

# **STIC Search Report**

## **Biotech-Chem Library**

**STIC Database Tracking Number: 130901**

**TO: Zohreh Fay**  
**Location: 3a61 / 3c70**  
**Wednesday, September 01, 2004**  
**Art Unit: 1614**  
**Phone: 272-0573**  
**Serial Number: 10 / 606501**

**From: Jan Delaval**  
**Location: Biotech-Chem Library**  
**Rem 1A51**  
**Phone: 272-2504**

**[jan.delaval@uspto.gov](mailto:jan.delaval@uspto.gov)**

### **Search Notes**

130901

Access DB#

## SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Zohreh Fay Examiner #: 66646 Date: 8/26/04  
 Att Unit: 1614 Phone Number: 301(571) 272-0573 Serial Number: 10/606,501  
 Mail Box and Bldg Room Location: \_\_\_\_\_ Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or quality of the invention. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: use of anecortave Acetate for the protection of  
visual Acuity in patients with age related Macular Degenerative  
 Inventors (please provide full names): \_\_\_\_\_

Earliest Priority Filing Date: 8/5/02

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

please search the claimed method of  
 composition and method of use.

## STAFF USE ONLY

	Type of Search	Vendors and cost where applicable
Searcher: <u>Jan</u>	NA Sequence (#) _____	STN <u>✓</u>
Searcher Phone #: <u>22504</u>	AA Sequence (#) _____	Dialog _____
Searcher Location _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: <u>9/1</u>	Bibliographic <u>✓</u>	Dr. Link _____
Date Completed: <u>9/11</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____
Technical Prep Time: <u>10</u>	Patent Family _____	WWW/Internet _____
Online Time: <u>35</u>	Other _____	Other (specify) _____

PTC 1594X (1)

=> fil reg

FILE 'REGISTRY' ENTERED AT 16:23:44 ON 01 SEP 2004

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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 31 AUG 2004 HIGHEST RN 736193-62-7

DICTIONARY FILE UPDATES: 31 AUG 2004 HIGHEST RN 736193-62-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d ide can l1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 7753-60-8 REGISTRY

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy-, 21-acetate (6CI, 7CI, 8CI)

OTHER NAMES:

CN 21-Acetoxypregna-4,9(11)-dien-17 $\alpha$ -ol-3,20-dione

CN Al 3789

CN Anecortave

CN Anecortave acetate

CN NSC 15475

CN NSC 24345

FS STEREOSEARCH

MF C23 H30 O5

LC STN Files: ADISINSIGHT, ADISNEWS, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDRUGNEWS, IMSRESEARCH, IPA, MRCK\*, PHAR, PROMT, PROUSDDR, PS, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL  
(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*

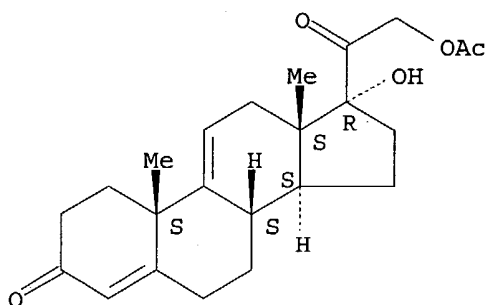
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

DT.CA Caplus document type: Dissertation; Journal; Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

89 REFERENCES IN FILE CA (1907 TO DATE)  
 89 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
 27 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

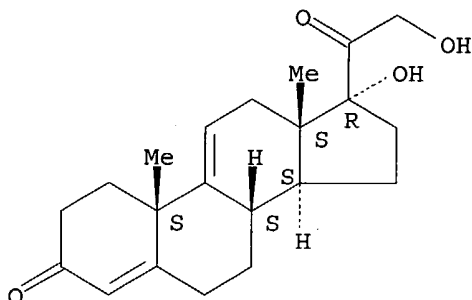
REFERENCE 1: 140:297513  
 REFERENCE 2: 140:157931  
 REFERENCE 3: 140:26949  
 REFERENCE 4: 139:265771  
 REFERENCE 5: 139:97753  
 REFERENCE 6: 139:53197  
 REFERENCE 7: 137:10999  
 REFERENCE 8: 134:91141  
 REFERENCE 9: 132:31278  
 REFERENCE 10: 132:520

=> d ide can 19

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 10184-70-0 REGISTRY  
 CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN 17,21-Dihydroxypregna-4,9(11)-diene-3,20-dione  
 CN AL 4940  
 FS STEREOSEARCH  
 MF C21 H28 O4  
 LC STN Files: BEILSTEIN\*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL  
 (\*File contains numerically searchable property data)  
 DT.CA Caplus document type: Journal; Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)  
 RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); RACT (Reactant or reagent)  
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);

PROC (Process); PRP (Properties); USES (Uses); NORL (No role in record)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

45 REFERENCES IN FILE CA (1907 TO DATE)  
 3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 45 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
 2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 140:157931  
 REFERENCE 2: 140:26949  
 REFERENCE 3: 139:97753  
 REFERENCE 4: 138:170402  
 REFERENCE 5: 132:31278  
 REFERENCE 6: 132:520  
 REFERENCE 7: 131:351535  
 REFERENCE 8: 131:54038  
 REFERENCE 9: 128:39554  
 REFERENCE 10: 120:164649

=> d his

(FILE 'HOME' ENTERED AT 16:07:03 ON 01 SEP 2004)  
 SET COST OFF

FILE 'REGISTRY' ENTERED AT 16:07:11 ON 01 SEP 2004  
 E ANECORTAVE/CN

L1 1 S E3,E4  
 SEL RN  
 L2 0 S E1/CRN

FILE 'HCAPLUS' ENTERED AT 16:08:35 ON 01 SEP 2004

L3 89 S L1  
 L4 10 S ANECORTAVE OR ANECORTAVE ACETATE OR NSC15475 OR NSC24345 OR N  
 L5 91 S L3,L4

L6 14 S L5 AND (EYE+OLD,NT,PFT,RT OR EYE, DISEASE+OLD,NT,PFT,RT)/CT  
L7 9 S L5 AND EYE#/CW (L) DISEASE  
L8 14 S L6,L7

FILE 'REGISTRY' ENTERED AT 16:11:26 ON 01 SEP 2004

L9 1 S 10184-70-0  
L10 0 S 10184-70-0/CRN

FILE 'HCAPLUS' ENTERED AT 16:11:47 ON 01 SEP 2004

L11 45 S L9  
L12 1 S AL4940 OR AL 4940  
L13 45 S L11,L12  
L14 8 S L13 AND (EYE+OLD,NT,PFT,RT OR EYE, DISEASE+OLD,NT,PFT,RT)/CT  
L15 6 S L13 AND EYE#/CW (L) DISEASE  
L16 16 S L8,L14,L15  
L17 119 S L5,L13  
L18 0 S L17 AND AMD  
L19 3 S L17 AND MACUL? DEGENER?  
L20 3 S L17 AND EYE, DISEASE/CT (L) (MACULA OR DEGEN? OR SENIL?)  
L21 16 S L16,L19-L20  
L22 13 S L21 NOT L19,L20  
E EYE+ALL/CT  
L23 184018 S E26+OLD,NT,PFT,RT OR E27+OLD,NT,PFT,RT OR E28+OLD,NT,PFT,RT  
L24 11 S L17 AND L23  
L25 3 S L24 AND L19,L20  
L26 8 S L24 NOT L25  
L27 13 S L22,L26  
L28 1 S US20040127472/PN OR (WO2003-US20154 OR US2002-401220#)/AP,PRN  
E JERDAN J/AU  
L29 7 S E4-E6  
E ZILLIOX P/AU  
L30 2 S E4  
E ROBERTSON S/AU  
L31 151 S E3,E15,E16  
E ROBERTSON STELLA/AU  
L32 20 S E3-E5  
L33 2 S L17 AND L28-L32  
E ALCO/PA,CS  
E ALCOM/PA,CS  
L34 877 S E3-E8 OR ALCON?/PA,CS  
L35 12 S L17 AND L34  
L36 19 S L19-L22,L27,L28,L35  
L37 19 S L36 AND L3-L8,L11-L36  
L38 18 S L37 AND (PD<=20020805 OR PRD<=20020805 OR AD<=20020805)  
L39 2 S L19,L20 AND L38  
L40 3 S L19,L20,L39  
L41 16 S L37-L38 NOT L40  
SEL DN AN 15 16  
L42 14 S L41 NOT E1-E6  
L43 1 S L33,L35 NOT L40,L42  
L44 16 S L41,L42

FILE 'REGISTRY' ENTERED AT 16:23:44 ON 01 SEP 2004

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 16:23:57 ON 01 SEP 2004

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FILE COVERS 1907 - 1 Sep 2004 VOL 141 ISS 10  
FILE LAST UPDATED: 31 Aug 2004 (20040831/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l44 all hitstr tot

L44 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 2002:428756 HCAPLUS  
DN 137:10999  
ED Entered STN: 07 Jun 2002  
TI Methods for reducing or preventing transplant rejection in the eye and intraocular implants for use therefor  
IN Wong, Vernon G.  
PA Oculex Pharmaceuticals, Inc., USA  
SO PCT Int. Appl., 33 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM A61L027-00  
CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002043785	A2	20020606	WO 2001-US44481	20011128 <--
	WO 2002043785	A3	20021121		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002036495	A5	20020611	AU 2002-36495	20011128 <--
	US 2002182185	A1	20021205	US 2001-997094	20011128 <--
	US 6699493	B2	20040302		
	EP 1339438	A2	20030903	EP 2001-986027	20011128 <--
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001015772	A	20040113	BR 2001-15772	20011128 <--
	JP 2004514702	T2	20040520	JP 2002-545755	20011128 <--
	US 2004137034	A1	20040715	US 2003-744560	20031222 <--
	JP 2004210798	A2	20040729	JP 2004-121618	20040416 <--
PRAI	US 2000-250023P	P	20001129	<--	
	US 2001-298253P	P	20010612	<--	
	JP 2002-545755	A3	20011128	<--	
	US 2001-997094	A1	20011128	<--	
	WO 2001-US44481	W	20011128	<--	

CLASS

PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

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WO 2002043785   ICM      A61L027-00
US 2002182185   ECLA     A61K009/00M16B
JP 2004514702   FTERM    4C076/AA51; 4C076/AA95; 4C076/BB24; 4C076/BB32;
                                4C076/CC07; 4C076/EE24A; 4C076/EE24M; 4C076/EE32A;
                                4C076/EE32M; 4C076/FF32; 4C084/AA02; 4C084/AA17;
                                4C084/BA44; 4C084/DA11; 4C084/MA02; 4C084/MA36;
                                4C084/MA58; 4C084/MA67; 4C084/NA10; 4C084/NA12;
                                4C084/ZB082; 4C084/ZC082; 4C086/AA01; 4C086/AA02;
                                4C086/DA10; 4C086/MA02; 4C086/MA03; 4C086/MA05;
                                4C086/MA07; 4C086/MA36; 4C086/MA58; 4C086/MA67;
                                4C086/NA10; 4C086/NA12; 4C086/ZB08
JP 2004210798   FTERM    4C076/AA67; 4C076/AA94; 4C076/BB24; 4C076/CC10;
                                4C076/CC29; 4C076/EE24A; 4C076/FF31; 4C086/AA01;
                                4C086/AA02; 4C086/DA10; 4C086/MA02; 4C086/MA05;
                                4C086/MA58; 4C086/NA12; 4C086/ZA33; 4C086/ZB21
AB  Methods for reducing or preventing transplant rejection in the eye of an
individual are described, comprising: (a) performing an ocular transplant
procedure; and (b) implanting in the eye a bioerodible drug delivery
system comprising an immunosuppressive agent and a bioerodible polymer.
Sustained-release intraocular implant containing HPMC 15, PLGA 35, and
dexamethasone 50% were prepared. The implants were implanted in the anterior
chamber of the rat eyes at the end of cornea transplants surgery. Rats
did not show any sign of rejection and the corneas stayed clear in all
eyes. After 8 wk the graft survival was 100%.
ST  transplant rejection eye intraocular implant; intraocular implant PLGA
dexamethasone transplant rejection
IT  Eye
    (anterior chamber; methods for reducing or preventing transplant
    rejection in eye and intraocular implants for use therefor)
IT  Polymers, biological studies
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    (bioerodible; methods for reducing or preventing transplant rejection
    in eye and intraocular implants for use therefor)
IT  Eye
    (cornea, transplant; methods for reducing or preventing transplant
    rejection in eye and intraocular implants for use therefor)
IT  Transplant and Transplantation
    (cornea; methods for reducing or preventing transplant rejection in eye
    and intraocular implants for use therefor)
IT  Human
    Immunosuppressants
    Transplant rejection
    (methods for reducing or preventing transplant rejection in eye and
    intraocular implants for use therefor)
IT  Polyesters, biological studies
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
    (Biological study); USES (Uses)
    (methods for reducing or preventing transplant rejection in eye and
    intraocular implants for use therefor)
IT  Eye
    (pigment epithelium, transplant; methods for reducing or preventing
    transplant rejection in eye and intraocular implants for use therefor)
IT  Intraocular lenses
    (sustained-release; methods for reducing or preventing transplant
    rejection in eye and intraocular implants for use therefor)
IT  50-02-2, Dexamethasone 50-24-8, Prednisolone 50-44-2, 6-Mercaptopurine
50-91-9, Floxuridine 51-21-8, Fluorouracil 54-25-1, 6-Azauridine
59-05-2, Methotrexate 89-38-3, Pteropterin 124-94-7, Triamcinolone
147-94-4, Cytarabine 154-42-7, Thioguanine 320-67-2, Azacitidine
426-13-1, Fluorometholone 446-86-6, Azathioprin 807-38-5, Fluocinolone
2668-66-8, Medrysone 3094-09-5, Doxifluridine 4291-63-8, Cladribine
5581-52-2, Thiamiprine 7753-60-8, Anecortave

```



**acetate** 9004-65-3, Hydroxypropyl methylcellulose 17902-23-7,  
 Tegafur 21679-14-1, Fludarabine 22006-84-4, Denopterin 31698-14-3,  
 Ancitabine 34346-01-5, Glycolic acid lactic acid copolymer 50924-49-7,  
 Mizoribine 52128-35-5, Trimetrexate 55726-47-1, Enocitabine  
 59865-13-3, Cyclosporin a 61422-45-5, Carmofur 72732-56-0, Piritrexim  
 80576-83-6, Edatrexate 95058-81-4, Gemcitabine 96187-53-0, Brequinar  
 98629-43-7, Gusperimus 104987-11-3, Tacrolimus 110690-43-2, Emitefur  
 112887-68-0, Tomudex

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(methods for reducing or preventing transplant rejection in eye and  
 intraocular implants for use therefor)

IT 7753-60-8, **Anecortave acetate**

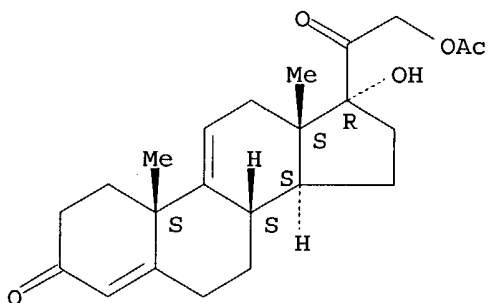
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(methods for reducing or preventing transplant rejection in eye and  
 intraocular implants for use therefor)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:25776 HCAPLUS

DN 134:91141

ED Entered STN: 11 Jan 2001

TI Combination therapy for lowering and controlling intraocular pressure  
 containing angiostatic steroids

IN Clark, Abbot F.

PA Alcon Laboratories, Inc., USA

SO U.S., 7 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-56

NCL 514179000

CC 63-6 (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6172054	B1	20010109	US 1995-491005	19950615 <--
PRAI	US 1995-491005		19950615	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6172054	ICM	A61K031-56
	NCL	514179000

OS MARPAT 134:91141

AB Angiostatic agents and another IOP lowering compound are combined in ophthalmic compns. to treat glaucoma and ocular hypertension. Methods for treating glaucoma and ocular hypertension are also disclosed. A solution was prepared contg timolol maleate and 4,9(11)-pregnadiene-17 $\alpha$ ,21-diol-3,20-dione 21 acetate.

ST glaucoma therapy angiostatic steroid; intraocular pressure angiostatic steroid compn

IT Adrenoceptor agonists  
Angiogenesis  
Antiglaucoma agents  
(combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

IT Prostaglandins  
Steroids, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

IT Drug delivery systems  
(solns., ophthalmic; combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

IT Adrenoceptor antagonists  
( $\beta$ -; combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

IT 53-02-1, Tetrahydrocortisol 57-63-6, 17 $\alpha$ -Ethinylestradiol  
7753-60-8 26839-75-8, Timolol 26921-17-5, Timolol maleate  
63659-18-7, Betaxolol 63659-19-8, Betaxolol hydrochloride 73218-79-8,  
Apraclonidine hydrochloride  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

IT 9001-03-0, Carbonic anhydrase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

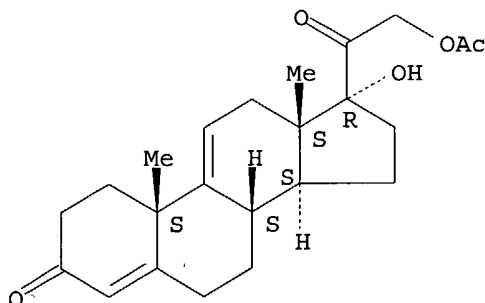
(1) Baldwin; US 4797413 1989 HCAPLUS  
(2) Bito; US 4599353 1986 HCAPLUS  
(3) Bondi; US 4730013 1988 HCAPLUS  
(4) Clark; US 4876250 1989 HCAPLUS  
(5) Clark; US 5371078 1994 HCAPLUS  
(6) Clark; IOVS 1994, V35(Suppl), P1057  
(7) Dean; US 5153192 1992 HCAPLUS  
(8) Dean; US 5240923 1993 HCAPLUS  
(9) Dean; US 5378703 1995 HCAPLUS  
(10) Ingber; Endocrinology 1986, V119, P1768 HCAPLUS  
(11) Jani; US 4911920 1990 HCAPLUS  
(12) Johnson; Mayo Clin Proc, Glaucoma:An Overview 1986, V61, P59 MEDLINE  
(13) Knepper; Pediat Neurosci 1985, V12, P240 HCAPLUS  
(14) Lang; US 5403841 1995 HCAPLUS  
(15) Lloyd; US 4540408 1985  
(16) Mazuel; US 4861760 1989 HCAPLUS  
(17) Missel; US 5212162 1993 HCAPLUS  
(18) Rohen; Ophthalmology 1983, V90(7) MEDLINE  
(19) Stjernschantz; US 5321128 1994 HCAPLUS  
(20) Woodward; US 5093329 1992 HCAPLUS

IT 7753-60-8  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:10622 HCAPLUS

DN 132:31278

ED Entered STN: 06 Jan 2000

TI Angiostatic steroids

IN Clark, Abbot F.; Conrow, Raymond E.

PA Alcon Laboratories, Inc., USA

SO U.S., 18 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM A01N045-00

ICS C07J053-00; C07J005-00; C07J007-00

NCL 514171000

CC 2-4 (Mammalian Hormones)

Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6011023	A	20000104	US 1997-924419	19970827 <--
PRAI	US 1997-924419		19970827	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6011023	ICM	A01N045-00
	ICS	C07J053-00; C07J005-00; C07J007-00
	NCL	514171000

AB Methods and compns. for preventing and treating neovascularization with angiostatic steroids is disclosed.

ST neovascularization angiostatic steroid delivery

IT Steroids, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Angiostatic steroids methods and compds. for prevention and treatment of neovascularization)

IT Blood vessel, disease

(Osler-Wever syndrome; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Blood vessel, neoplasm

(angiofibroma; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Anti-inflammatory agents

Arteriosclerosis

Arthritis

Burn

- Eye
  - Granulation
  - Neoplasm
  - Psoriasis
    - (angiostatic steroids methods and compns. for prevention and treatment of **neovascularization**)
- IT Blood vessel, disease
  - (arteriovenous malformation; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Eye
  - (cornea, graft; angiostatic steroids methods and compns. for prevention and treatment of **neovascularization**)
- IT Eye
  - (cornea; angiostatic steroids methods and compns. for prevention and treatment of **neovascularization**)
- IT Wound healing
  - (delayed; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Eye, disease
  - (**diabetic retinopathy**; angiostatic steroids methods and compns. for prevention and treatment of **neovascularization**)
- IT Joint, anatomical
  - (disease, hemophilic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Bone, disease
  - (fracture, nonunion; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Blood vessel, neoplasm
  - (hemangioma; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Shock (circulatory collapse)
  - (hemorrhagic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Skin, disease
  - (hypertrophic scar; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Drug delivery systems
  - (injections, ophthalmic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Glaucoma (disease)
  - (neovascular; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Angiogenesis
  - (neovascularization; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Granuloma
  - (pyogenic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Eye, disease
  - (**retrolental fibroplasia**; angiostatic steroids methods and compns. for prevention and treatment of **neovascularization**)
- IT Connective tissue
  - (scleroderma; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Shock (circulatory collapse)
  - (septic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Neoplasm
  - (solid and pterigium; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- IT Drug delivery systems

(solns., ophthalmic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization` )

IT Brain, disease  
(stroke; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Drug delivery systems  
(suspensions, ophthalmic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Drug delivery systems  
(topical; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Eye, disease  
(trachoma; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Head  
Spinal cord  
(trauma; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Shock (circulatory collapse)  
(traumatic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Adhesion, physical  
(vascular; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT 149916-70-1P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT 149916-61-0P 149916-69-8P 160964-90-9P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT 53-02-1 57-63-6 68-23-5 68-60-0, Tetrahydrocortexolone 68-96-2, 17 $\alpha$ -Hydroxyprogesterone 302-91-0 302-97-6 566-35-8, 11-Epicortisol 641-84-9 651-43-4 7753-60-8  
10184-70-0 15734-50-6 149916-56-3 149916-57-4 149916-59-6  
149916-60-9 149916-62-1 149916-64-3 149916-65-4 149916-67-6  
149952-80-7 149952-81-8 150213-68-6 160964-92-1, 21-Nor-5 $\beta$ -pregn-17(20)en-3 $\alpha$ ,16-diol 252684-24-5 252684-25-6  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT 58479-61-1  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT 149916-71-2P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

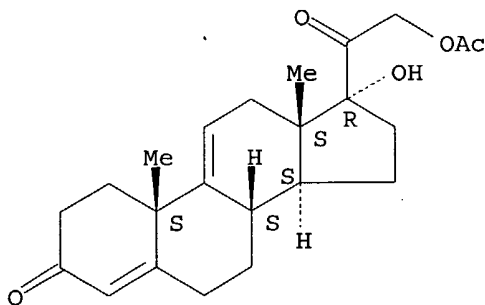
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

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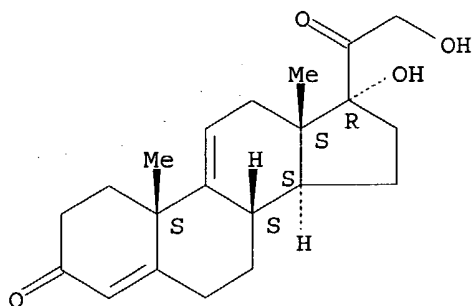
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 (30) Tokida; The Journal of Biological Chemistry 1990, V264(30), P18123
- IT 7753-60-8 10184-70-0  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
- RN 7753-60-8 HCAPLUS  
 CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



- RN 10184-70-0 HCAPLUS  
 CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1999:748307 HCAPLUS  
 DN 131:351535  
 ED Entered STN: 25 Nov 1999  
 TI synthesis and compositions of angiostatic agents for controlling ocular hypertension  
 IN Clark, Abbot F.  
 PA Alcon Laboratories, Inc., USA  
 SO U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 990,424, abandoned.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 IC ICM A61K031-58  
 ICS A61K031-56  
 NCL 514172000  
 CC 32-5 (Steroids)  
 Section cross-reference(s): 1, 63

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5990099	A	19991123	US 1997-994114	19971219 <--
	US 4876250	A	19891024	US 1988-264918	19881031 <--
	US 5371078	A	19941206	US 1992-941485	19920908 <--
	US 5698545	A	19971216	US 1996-643387	19960506 <--
	WO 9903503	A1	19990128	WO 1998-US12711	19980618 <--
	W: AU, BR, CA, JP, MX, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9881515	A1	19990210	AU 1998-81515	19980618 <--
	AU 734195	B2	20010607		
	EP 1003553	A1	20000531	EP 1998-931367	19980618 <--
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	JP 2001510170	T2	20010731	JP 2000-502798	19980618 <--
	CA 2315829	AA	19990701	CA 1998-2315829	19981207 <--
	WO 9932127	A1	19990701	WO 1998-US25913	19981207 <--
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	AU 734436	B2	20010614		
	EP 1039912	A1	20001004	EP 1998-961956	19981207 <--
	EP 1039912	B1	20020807		
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	BR 9813684	A	20001010	BR 1998-13684	19981207 <--
	JP 2001526233	T2	20011218	JP 2000-525118	19981207 <--

AT 221781	E	20020815	AT 1998-961956	19981207 <--
ES 2177112	T3	20021201	ES 1998-961956	19981207 <--
PT 1039912	T	20021231	PT 1998-961956	19981207 <--
MX 9911140	A	20000430	MX 1999-11140	19991202 <--
HK 1029922	A1	20021025	HK 2001-100647	20010129 <--
PRAI US 1988-264918	A1	19881031	<--	
US 1989-419226	B2	19891010	<--	
US 1990-559123	B2	19900727	<--	
US 1992-941485	A1	19920908	<--	
US 1994-349342	B1	19941202	<--	
US 1996-643387	A1	19960506	<--	
US 1997-990424	B2	19971215	<--	
US 1997-895184	A	19970716	<--	
US 1997-994114	A	19971219	<--	
WO 1998-US12711	W	19980618	<--	
WO 1998-US25913	W	19981207	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 5990099	ICM	A61K031-58
	ICS	A61K031-56
	NCL	514172000
US 5990099	ECLA	A61K031/56; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00 <--
US 5371078	ECLA	A61K031/56; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00 <--
US 5698545	ECLA	A61K031/565; A61K031/565; A61K031/565T10; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/57; A61K031/57L5; A61K031/58 <--
WO 9932127	ECLA	A61K031/00; A61K031/56; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00 <--
OS	MARPAT 131:351535	
AB	Compsn. of angiostatic agents for treating GLC1A glaucoma and methods for their use are disclosed. Preparation of selected steroid agents of the invention, e.g. 3 $\beta$ -acetamido-5 $\beta$ -pregnan-11 $\beta$ ,17 $\alpha$ ,21-triol-20-one 21-acetate, is described.	
ST	GLC1A glaucoma steroid angiostatic agent prepn	
IT	Angiogenesis inhibitors	
	Antiglaucoma agents	
	(synthesis and compns. of angiostatic agents for controlling ocular hypertension)	
IT	149916-69-8P	
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)	
	(synthesis and compns. of angiostatic agents for controlling ocular hypertension)	
IT	7753-60-8P 10184-70-0P	149916-61-0P 149916-70-1P
	199583-00-1P	
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)	
	(synthesis and compns. of angiostatic agents for controlling ocular hypertension)	



IT 53-02-1, Tetrahydrocortisol  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(synthesis and compns. of angiostatic agents for controlling ocular hypertension)

IT 149916-71-2P 150213-49-3P 150213-50-6P 160896-36-6P 160964-93-2P  
250661-72-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis and compns. of angiostatic agents for controlling ocular hypertension)

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

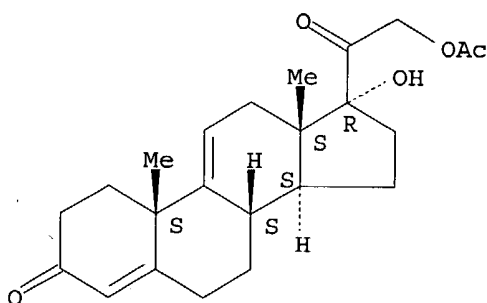
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IT 7753-60-8P 10184-70-0P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(synthesis and compns. of angiostatic agents for controlling ocular hypertension)

RN 7753-60-8 HCAPLUS

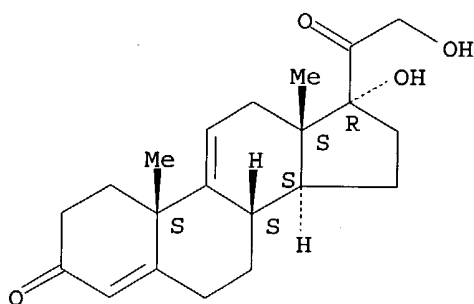
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 10184-70-0 HCAPLUS  
 CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1999:672339 HCAPLUS  
 DN 132:520  
 ED Entered STN: 22 Oct 1999  
 TI Angiostatic activity of steroids in the chick embryo CAM and rabbit cornea models of neovascularization  
 AU McNatt, Loretta G.; Weimer, Lori; Yanni, John; Clark, Abbot F.  
 CS Alcon Laboratories, Inc., Fort Worth, TX, USA  
 SO Journal of Ocular Pharmacology and Therapeutics (1999), 15(5), 413-423  
 CODEN: JOPTFU; ISSN: 1080-7683  
 PB Mary Ann Liebert, Inc.  
 DT Journal  
 LA English  
 CC 2-2 (Mammalian Hormones)  
 Section cross-reference(s): 12  
 AB Ocular neovascular diseases represent a major cause of blindness in the world. Angiostatic steroids are a unique class of compds. which inhibit the formation of new blood vessels in various models, including ocular models of angiogenesis. In search of potent new anti-angiogenic agents for the treatment of ocular neovascular disease, a large group of steroids were evaluated for angiostatic activity in the chick embryo CAM model. Angiostatic activity was found among all steroid classes included in the study. There was a good correlation between the angiostatic efficacies of 15 diverse steroids tested in the chick CAM and in the rabbit LPS-induced corneal pocket models of neovascularization ( $r=0.76$ ,  $p=0.01$ ). These studies show that potent angiostatic steroids inhibit neovascularization in two different animal models, suggesting a common mechanism of action. Glucocorticoid therapy is sometimes associated with ocular side effects. Two

of the most potent angiostatic steroids, **AL-3789** and **AL-4940**, were evaluated for glucocorticoid-mediated anti-inflammatory activity in the in vitro U937 cell model of LPS-induced IL-1 induction and found to be devoid of glucocorticoid activity.

Angiostatic steroids which lack glucocorticoid activity should be attractive drug candidates for treating ocular neovascular disease.

- ST steroid **AL3789** angiostatic structure activity  
neovascularization; **AL4940** steroid angiostatic structure  
activity neovascularization; glucocorticoid antiinflammatory steroid  
angiostatic neovascularization; chicken rabbit neovascularization model  
steroid angiostatic
- IT Angiogenesis inhibitors  
Anti-inflammatory agents  
Chicken (*Gallus domesticus*)  
Embryo, animal  
(angiostatic activity of steroids in chick embryo CAM and rabbit cornea  
models of neovascularization)
- IT Glucocorticoids  
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or  
effector, except adverse); BSU (Biological study, unclassified); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(angiostatic activity of steroids in chick embryo CAM and rabbit cornea  
models of neovascularization)
- IT Structure-activity relationship  
(angiostatic; angiostatic activity of steroids in chick embryo CAM and  
rabbit cornea models of neovascularization)
- IT **Eye**  
(cornea; angiostatic activity of steroids in chick embryo CAM and  
rabbit cornea models of **neovascularization**)
- IT Angiogenesis  
Angiogenesis  
(neovascularization, eye; angiostatic activity of steroids in chick  
embryo CAM and rabbit cornea models of neovascularization)
- IT **Eye, disease**  
(**neovascularization**; angiostatic activity of steroids in  
chick embryo CAM and rabbit cornea models of **neovascularization**  
)
- IT 7753-60-8, **AL-3789 10184-70-0**,  
**AL 4940**  
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or  
effector, except adverse); BSU (Biological study, unclassified); PRP  
(Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(angiostatic activity of steroids in chick embryo CAM and rabbit cornea  
models of neovascularization)
- IT 50-02-2, Dexamethasone 50-23-7, Cortisol 50-24-8, Prednisolone  
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or  
effector, except adverse); BSU (Biological study, unclassified); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(angiostatic activity of steroids in chick embryo CAM and rabbit cornea  
models of neovascularization)
- IT 50-28-2, 17 $\beta$ -Estradiol, biological studies 53-02-1 57-63-6,  
17 $\alpha$ -Ethinylestradiol 58-18-4, 17 $\alpha$ -Methyltestosterone  
58-22-0, Testosterone 68-22-4, Norethindrone 68-23-5, Norethynodrel  
68-42-8 68-60-0 72-33-3, Mestranol 302-91-0, AL 3308 302-97-6, AL  
3793 362-07-2, 2-Methoxyestradiol 434-03-7, Ethisterone 520-85-4,  
Medroxyprogesterone 641-84-9, AL 3841 1516-47-8, AL 3685 88729-26-4,  
AL 3855 105384-40-5, U-42129 111320-97-9, U 73843 149916-54-1, AL  
3913 149916-56-3, AL 3914 149916-59-6, AL 4989 149916-62-1, AL 4988  
149916-69-8, AL 4063 149916-70-1, AL 3806 251297-08-2, AL 4710  
251297-11-7, U 87096 251297-13-9, AL 4772 251297-16-2, AL 5267  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(angiostatic activity of steroids in chick embryo CAM and rabbit cornea models of neovascularization)

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- (24) Miller, J; Ophthalmology 1993, V100, P9 MEDLINE
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- (27) Pepper, M; J Cell Biochem 1994, V55, P419 HCAPLUS
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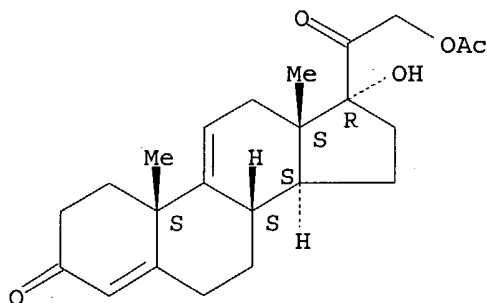
IT 7753-60-8, AL-3789 10184-70-0,  
AL 4940

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(angiostatic activity of steroids in chick embryo CAM and rabbit cornea models of neovascularization)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

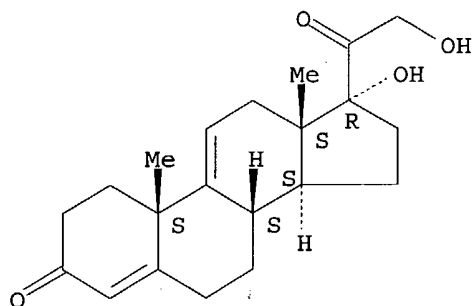


RN 10184-70-0 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA

INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1999:425760 HCAPLUS  
 DN 131:54038  
 ED Entered STN: 09 Jul 1999  
 TI Steroidal angiostatic agents and compositions for controlling GLC1A  
 glaucoma, compositions, and preparation thereof  
 IN Clark, Abbot F.  
 PA Alcon Laboratories, Inc., USA  
 SO PCT Int. Appl., 35 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-57  
 ICS A61K031-575; A61K031-56  
 CC 1-12 (Pharmacology)  
 Section cross-reference(s): 2, 32, 63

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9932127	A1	19990701	WO 1998-US25913	19981207 <--
	W: AU, BR, CA, JP, MX				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5990099	A	19991123	US 1997-994114	19971219 <--
	WO 9903503	A1	19990128	WO 1998-US12711	19980618 <--
	W: AU, BR, CA, JP, MX, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9881515	A1	19990210	AU 1998-81515	19980618 <--
	AU 734195	B2	20010607		
	EP 1003553	A1	20000531	EP 1998-931367	19980618 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9811012	A	20001017	BR 1998-11012	19980618 <--
	JP 2001510170	T2	20010731	JP 2000-502798	19980618 <--
	CA 2315829	AA	19990701	CA 1998-2315829	19981207 <--
	AU 9917142	A1	19990712	AU 1999-17142	19981207 <--
	AU 734436	B2	20010614		
	EP 1039912	A1	20001004	EP 1998-961956	19981207 <--
	EP 1039912	B1	20020807		
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	BR 9813684	A	20001010	BR 1998-13684	19981207 <--
	JP 2001526233	T2	20011218	JP 2000-525118	19981207 <--
	AT 221781	E	20020815	AT 1998-961956	19981207 <--

	MX 9911140	A	20000430	MX 1999-11140	19991202 <--
	HK 1029922	A1	20021025	HK 2001-100647	20010129 <--
PRAI	US 1997-994114	A	19971219	<--	
	US 1988-264918	A1	19881031	<--	
	US 1989-419226	B2	19891010	<--	
	US 1990-559123	B2	19900727	<--	
	US 1992-941485	A1	19920908	<--	
	US 1994-349342	B1	19941202	<--	
	US 1996-643387	A1	19960506	<--	
	US 1997-895184	A	19970716	<--	
	US 1997-990424	B2	19971215	<--	
	WO 1998-US12711	W	19980618	<--	
	WO 1998-US25913	W	19981207	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9932127	ICM	A61K031-57
	ICS	A61K031-575; A61K031-56
WO 9932127	ECLA	A61K031/00; A61K031/56; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00 <--
US 5990099	ECLA	A61K031/56; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00 <--
OS	MARPAT 131:54038	
AB	Compns. of steroid angiostatic agents for treating GLC1A glaucoma and methods for their use are disclosed. Preparation of selected steroid agents of the invention, e.g. 3 $\beta$ -acetamido-21-acetoxy-5 $\beta$ -pregnan-11 $\beta$ ,17 $\alpha$ -diol-20-one, is described.	
ST	GLC1A glaucoma steroid angiostatic agent prepn	
IT	Gene, animal	
	RL: BSU (Biological study, unclassified); BIOL (Biological study) (GLC1A; steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)	
IT	Angiogenesis inhibitors	
	Antiglaucoma agents	
	Drug delivery systems (steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)	
IT	149916-71-2P	150213-50-6P
	RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and reaction; steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)	
IT	53-02-1	6160-65-2, Thiocarbonyl diimidazole 58479-61-1
	RL: RCT (Reactant); RACT (Reactant or reagent) (reaction; steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)	
IT	149916-69-8P	
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)	
IT	149916-61-0P	149916-70-1P 199583-00-1P
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (steroidal angiostatic agents and compns. for controlling GLC1A	

glaucoma, compns., and preparation)

IT 7753-60-8 10184-70-0  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)

IT 228397-21-5P  
 RL: BYP (Byproduct); PREP (Preparation)  
 (steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

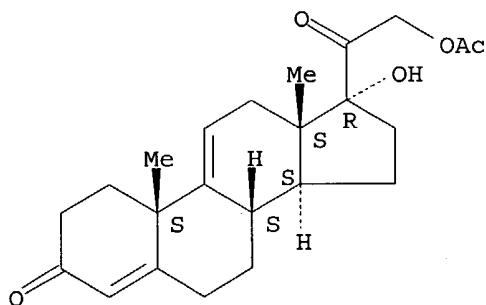
- (1) Alcon Lab Inc; WO 9310141 A 1993 HCAPLUS
- (2) Clark Abbot, F; US 4876250 A 1989 HCAPLUS
- (3) Clark Abbot, F; US 5371078 A 1994 HCAPLUS
- (4) Clark Abbot, F; US 5698545 A 1997 HCAPLUS
- (5) Univ Duke; WO 9518621 A 1995 HCAPLUS
- (6) Upjohn Co; WO 9119731 A 1991 HCAPLUS

IT 7753-60-8 10184-70-0  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

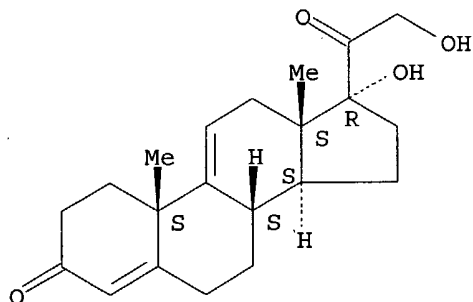
Absolute stereochemistry.



RN 10184-70-0 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 1997:795450 HCAPLUS  
DN 128:136567  
ED Entered STN: 20 Dec 1997  
TI **AL-3789**: a novel ophthalmic angiostatic steroid  
AU Clark, Abbot F.  
CS **Alcon Lab., Fort worth, TX, 76134, USA**  
SO Expert Opinion on Investigational Drugs (1997), 6(12), 1867-1877  
CODEN: EOIDER; ISSN: 0967-8298  
PB Ashley Publications  
DT Journal; General Review  
LA English  
CC 2-0 (Mammalian Hormones)  
Section cross-reference(s): 1  
AB A review with 27 refs. Ocular neovascular diseases are a leading cause of blindness in the world. Research is beginning to unravel the complex mechanisms involved in the pathogenesis of ocular neovascular diseases, but currently there are very few methods for the effective treatment of these blinding disorders. **AL-3789** (Alcon Labs.) is an angiostatic steroid which shows significant activity in inhibiting new blood vessel formation in a wide variety of models of neovascularization, including neovascularization in ocular tissues. This angiostatic steroid has broad angiostatic activity and is effective in a number of different animal species and tissues, regardless of the angiogenic stimulus. **AL-3789** is devoid of conventional steroid hormone activity and does not appear to have any other pharmacol. side-effects at the doses and routes of administration tested. In preclin. safety studies, **AL-3789** has no apparent ocular or systemic toxicity when dosed chronically by topical ocular or by systemic administration. It remains to be seen whether these promising results will be confirmed in clin. studies.  
ST review angiostatic **AL 3789** ocular neovascularization  
IT Angiogenesis inhibitors  
    **Eye**  
        (**AL-3789** as a novel ophthalmic angiostatic steroid for treatment of ocular disorders resulting from neovascularization)  
IT Angiogenesis  
    (neovascularization; **AL-3789** as a novel ophthalmic angiostatic steroid for treatment of ocular disorders resulting from neovascularization)  
IT 7753-60-8, **AL 3789**  
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
        (**AL-3789** as a novel ophthalmic angiostatic steroid for treatment of ocular disorders resulting from neovascularization)  
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE  
    (1) Adamis, A; Arch Ophthalmol 1996, V114, P66 HCAPLUS  
    (2) Aiello, L; Arch Ophthalmol 1996, V114(10), P1252 MEDLINE  
    (3) Aiello, L; Proc Natl Acad Sci USA 1995, V92(23), P10457 HCAPLUS  
    (4) Ashino-Fuse, H; Int J Cancer 1989, V44, P859 HCAPLUS  
    (5) Avery, R; Arch Ophthalmol 1990, V108, P1474 MEDLINE  
    (6) Benezra, D; Invest Ophthalmol Vis Sci 1997, V38, P1954 MEDLINE  
    (7) Blei, F; J Cell Physiol 1993, V155, P568 HCAPLUS  
    (8) Clark, A; Invest Ophthalmol Vis Sci 1994, V35(4), P2734  
    (9) Clark, A; J Glaucoma 1995, V4, P354  
    (10) Crum, R; Science 1985, V230, P1375 HCAPLUS  
    (11) Danis, R; Invest Ophthalmol Vis Sci 1997, V38(4), PS964  
    (12) D'Amato, R; Proc Natl Acad Sci USA 1994, V91, P4082 HCAPLUS  
    (13) Folkman, J; New Engl J Med 1995, V333, P1757 MEDLINE



- (14) Friedlander, M; Proc Natl Acad Sci USA 1996, V93, P9764 HCAPLUS  
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 (17) Guyer, D; Arch Ophthalmol 1997, V115, P865  
 (18) Kusaka, M; Biochem Biophys Res Comm 1991, V174, P1070 HCAPLUS  
 (19) LI, W; Invest Ophthalmol Vis Sci 1991, V32, P2898 MEDLINE  
 (20) Ma, D; Invest Ophthalmol Vis Sci 1995, V36(4), P2265  
 (21) McNatt, L; J Steroid Biochem Mol Biol 1992, V42(7), P687 HCAPLUS  
 (22) Miller, J; Ophthalmology 1993, V100, P9 MEDLINE  
 (23) Proia, A; Exp Eye Res 1993, V57, P693 HCAPLUS  
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 (25) Shima, D; Mol Med 1995, V1(2), P182 HCAPLUS  
 (26) Smith, L; Science 1997, V276, P1706 HCAPLUS  
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IT 7753-60-8, AL 3789

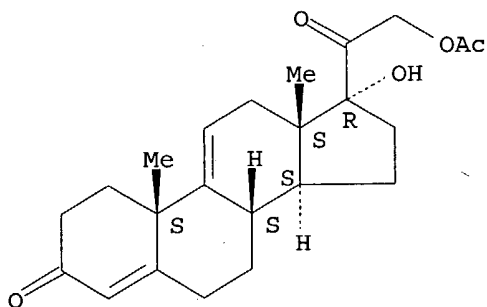
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(AL-3789 as a novel ophthalmic angiostatic steroid  
 for treatment of ocular disorders resulting from neovascularization)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:745948 HCAPLUS

DN 128:39554

ED Entered STN: 27 Nov 1997

TI Use of steroid compounds to prevent non-cancerous tissue growth

IN Clark, Abbot F.; Goode, Stephen M.

PA Alcon Laboratories, Inc., USA

SO PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-565

ICS A61K031-57

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 2

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9741867	A1	19971113	WO 1997-US2809	19970221 <--
	W: AU, CA, JP, MX				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9719701	A1	19971126	AU 1997-19701	19970221 <--
PRAI	US 1996-19060P	P	19960509	<--	

WO 1997-US2809 W 19970221 &lt;--

## CLASS

PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

WO 9741867 ICM A61K031-565  
ICS A61K031-57

OS MARPAT 128:39554

AB Disclosed are pregnane analogs for use in preventing non-cancerous tissue growth and pharmaceutical compns. containing them. For example, an ocular solution contained 21-nor-5 $\beta$ -pregnan-3 $\alpha$ ,17 $\alpha$ ,20-triol-3-phosphate 1, benzalkonium chlorides 0.01, HPMC 0.5, NaCl 0.8, Na phosphate 0.28, di-Na edetate 0.01 %, NaOH/HCl q.s. to pH 7.2, and purified water to 100 %.

ST pregnane steroid noncancerous tissue growth prevention

IT **Glaucoma (disease)**

(filtration bleb failure; steroids for prevention of noncancerous tissue growth)

IT Keratosis

(hyperkeratosis; steroids for prevention of noncancerous tissue growth)

IT Drug delivery systems

(ointments, creams; steroids for prevention of noncancerous tissue growth)

IT Drug delivery systems

(ointments; steroids for prevention of noncancerous tissue growth)

IT Neoplasm

(polyps; steroids for prevention of noncancerous tissue growth)

IT **Eye, disease**

(pterygium; steroids for prevention of noncancerous tissue growth)

IT Drug delivery systems

(solns., ophthalmic; steroids for prevention of noncancerous tissue growth)

IT Keloid

Wound healing

(steroids for prevention of noncancerous tissue growth)

IT Progestogens

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(steroids for prevention of noncancerous tissue growth)

IT Drug delivery systems

(suppositories; steroids for prevention of noncancerous tissue growth)

IT Drug delivery systems

Drug delivery systems

(suspensions, ophthalmic; steroids for prevention of noncancerous tissue growth)

IT Drug delivery systems

(tablets; steroids for prevention of noncancerous tissue growth)

IT 57-63-6 68-23-5 302-97-6 7753-60-8 10184-70-0

149916-54-1 149916-55-2 149916-56-3 149916-57-4 149916-58-5

149916-59-6 149916-60-9 149916-62-1 149916-69-8 199583-00-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(steroids for prevention of noncancerous tissue growth)

IT 7753-60-8 10184-70-0

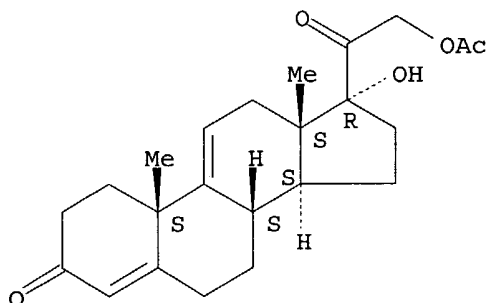
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(steroids for prevention of noncancerous tissue growth)

RN 7753-60-8 HCAPLUS

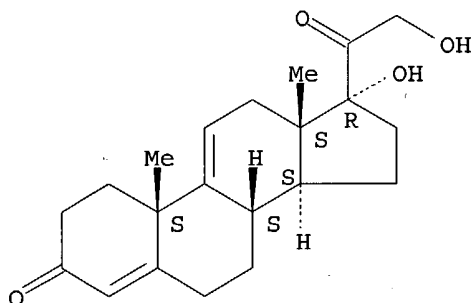
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 10184-70-0 HCAPLUS  
 CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1997:704225 HCAPLUS  
 DN 128:57124  
 ED Entered STN: 08 Nov 1997  
 TI Mechanism of action and clinical efficacy of **AL-3789**,  
 an angiostatic steroid (neovascularization, pterygium, tumor growth)  
 AU Defaller, Joseph Michael  
 CS Health Science Center, Univ. of North Texas, Fort Worth, TX, USA  
 SO (1996) 115 pp. Avail.: UMI, Order No. DA9735970  
 From: Diss. Abstr. Int., B 1997, 58(6), 2974  
 DT Dissertation  
 LA English  
 CC 1-6 (Pharmacology)  
 AB Unavailable  
 ST **AL3789** steroid angiostasis neovascularization tumor pterygium  
 IT Angiogenesis inhibitors  
 Antitumor agents  
 (angiostatic steroid **AL-3789** mechanism and clin.  
 efficacy)  
 IT Angiogenesis  
 (neovascularization; angiostatic steroid **AL-3789**  
 mechanism and clin. efficacy)  
 IT **Eye, disease**  
 (pterygium; angiostatic steroid **AL-3789** mechanism  
 and clin. efficacy)  
 IT 7753-60-8, **AL 3789**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)

(angiostatic steroid **AL-3789** mechanism and clin. efficacy)IT 7753-60-8, **AL 3789**

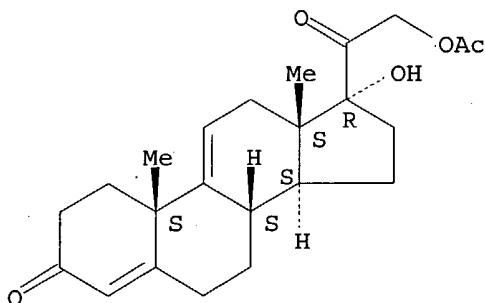
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(angiostatic steroid **AL-3789** mechanism and clin. efficacy)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:294615 HCAPLUS

DN 122:114929

ED Entered STN: 14 Jan 1995

TI Angiostatic steroids and methods and compositions for controlling ocular hypertension

IN Clark, Abbot F.; Conrow, Raymond E.

PA Alcon Laboratories, Inc., USA

SO U.S., 10 pp. Cont.-in-part of U.S. Ser. No. 559, 123, abandoned.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-56

NCL 514182000

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 32

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5371078	A	19941206	US 1992-941485	19920908 <--
	US 4876250	A	19891024	US 1988-264918	19881031 <--
	WO 9310141	A2	19930527	WO 1992-US10133	19921123 <--
	WO 9310141	A3	19930902		
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
	AU 9332235	A1	19930615	AU 1993-32235	19921123 <--
	AU 678961	B2	19970619		
	EP 614463	A1	19940914	EP 1993-900609	19921123 <--
	EP 614463	B1	20030212		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
	JP 07501081	T2	19950202	JP 1993-509563	19921123 <--
	JP 3378245	B2	20030217		
	EP 1236469	A2	20020904	EP 2002-9991	19921123 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE				

EP 1236470	A2	20020904	EP 2002-9992	19921123 <--
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EP 1236471	A2	20020904	EP 2002-9993	19921123 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE				
AT 232540	E	20030215	AT 1993-900609	19921123 <--
ES 2187503	T3	20030616	ES 1993-900609	19921123 <--
US 5698545	A	19971216	US 1996-643387	19960506 <--
US 5990099	A	19991123	US 1997-994114	19971219 <--
WO 9903503	A1	19990128	WO 1998-US12711	19980618 <--
W: AU, BR, CA, JP, MX, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9881515	A1	19990210	AU 1998-81515	19980618 <--
AU 734195	B2	20010607		
EP 1003553	A1	20000531	EP 1998-931367	19980618 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9811012	A	20001017	BR 1998-11012	19980618 <--
JP 2001510170	T2	20010731	JP 2000-502798	19980618 <--
HK 1012638	A1	20030509	HK 1998-113831	19981217 <--
MX 9911140	A	20000430	MX 1999-11140	19991202 <--
PRAI US 1988-264918	A1	19881031	<--	
US 1989-419226	B2	19891010	<--	
US 1990-559123	B2	19900727	<--	
US 1991-796169	A	19911122	<--	
US 1992-892448	A	19920602	<--	
US 1992-941485	A	19920908	<--	
EP 1993-900609	A3	19921123	<--	
WO 1992-US10133	A	19921123	<--	
US 1994-349342	B1	19941202	<--	
US 1996-643387	A1	19960506	<--	
US 1997-895184	A	19970716	<--	
US 1997-990424	B2	19971215	<--	
WO 1998-US12711	W	19980618	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 5371078	ICM	A61K031-56
	NCL	514182000
US 5371078	ECLA	A61K031/56; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00 <--
EP 1236469	ECLA	A61K031/56; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/565 <--
US 5698545	ECLA	A61K031/565; A61K031/565; A61K031/565T10; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/57; A61K031/57L5; A61K031/58 <--
US 5990099	ECLA	A61K031/56; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00 <--

OS MARPAT 122:114929

AB Pharmaceutical compns. of the angiostatic steroids and methods for their use in treating ocular hypertension, including controlling the ocular hypertension associated with primary open-angle glaucoma, are disclosed. In addition, the combination of the compds. with glucocorticoids for the prevention of elevated IOP during the treatment of inflammation is disclosed. For example, 21-methyl-5 $\beta$ -pregnan-3 $\alpha$ ,11 $\beta$ ,17 $\alpha$ ,21-tetrol-20-one 21-Me ether (I) was prepared

from tetrahydrocortisol F. An ophthalmic composition contained I 1.0, tyloxapol 0.01-0.05, HPMC 0.5, benzalkonium chloride 0.01, NaCl 0.8, di-Na edetate 0.01%, NaOH/HCl q.s. to pH 7.4, and purified water to 100 mL.

ST ophthalmic angiostatic steroid glaucoma; ocular hypertension angiogenesis inhibitor steroid

IT Steroids, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(angiostatic steroids for controlling ocular hypertension)

IT Inflammation inhibitors  
(glucocorticoids; angiostatic steroids for prevention of elevated intraocular pressure during treatment of inflammation)

IT Corticosteroids, biological studies  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(gluco-, angiostatic steroids for prevention of elevated intraocular pressure during treatment of inflammation)

IT Pharmaceutical dosage forms  
(ophthalmic, angiostatic steroids for controlling ocular hypertension)

IT **Glaucoma (disease)**  
(primary open-angle, angiostatic steroids for controlling ocular hypertension)

IT 160964-90-9P  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(angiostatic steroids for controlling ocular hypertension)

IT 57-63-6 68-23-5 302-97-6 641-84-9 **7753-60-8** 149916-54-1  
149916-56-3 149916-57-4 149916-59-6 149916-60-9 149916-61-0  
149916-62-1 149916-64-3 149916-65-4 149916-66-5 149916-67-6  
149916-69-8 149952-80-7 149952-81-8 150213-68-6 160896-34-4  
160964-91-0 160964-92-1  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(angiostatic steroids for controlling ocular hypertension)

IT 50-02-2, Dexamethasone  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(angiostatic steroids for prevention of elevated intraocular pressure during treatment of inflammation)

IT 53-02-1, Tetrahydrocortisol 58479-61-1, tert-Butyldiphenylchlorosilane  
149916-69-8  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of angiostatic steroids for controlling ocular hypertension)

IT 149916-71-2P 150213-49-3P 150213-50-6P 160896-36-6P 160964-93-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of angiostatic steroids for controlling ocular hypertension)

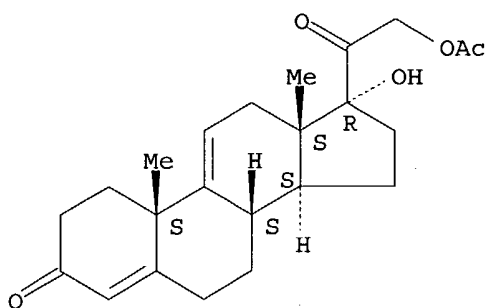
IT 149916-70-1P  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of angiostatic steroids for controlling ocular hypertension)

IT **7753-60-8**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(angiostatic steroids for controlling ocular hypertension)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1993:560646 HCAPLUS  
 DN 119:160646  
 ED Entered STN: 16 Oct 1993  
 TI Preparation and formulation of angiostatic steroids  
 IN Clark, Abbot F.; Conrow, Raymond E.  
 PA **Alcon Laboratories, Inc., USA**  
 SO PCT Int. Appl., 54 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07J005-00  
 ICS A61K031-56; C07J003-00; C07J051-00; C07J011-00; C07J009-00;  
 C07J041-00  
 CC 32-5 (Steroids)  
 Section cross-reference(s): 1, 63

## FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9310141	A2	19930527	WO 1992-US10133	19921123 <--
	WO 9310141	A3	19930902		
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
	US 5371078	A	19941206	US 1992-941485	19920908 <--
	AU 9332235	A1	19930615	AU 1993-32235	19921123 <--
	AU 678961	B2	19970619		
	EP 614463	A1	19940914	EP 1993-900609	19921123 <--
	EP 614463	B1	20030212		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
	JP 07501081	T2	19950202	JP 1993-509563	19921123 <--
	JP 3378245	B2	20030217		
	AT 232540	E	20030215	AT 1993-900609	19921123 <--
	US 5679666	A	19971021	US 1994-342524	19941121 <--
	US 5770592	A	19980623	US 1997-895184	19970716 <--
	WO 9903503	A1	19990128	WO 1998-US12711	19980618 <--
	W: AU, BR, CA, JP, MX, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9881515	A1	19990210	AU 1998-81515	19980618 <--
	AU 734195	B2	20010607		
	EP 1003553	A1	20000531	EP 1998-931367	19980618 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9811012	A	20001017	BR 1998-11012	19980618 <--
	JP 2001510170	T2	20010731	JP 2000-502798	19980618 <--
	HK 1012638	A1	20030509	HK 1998-113831	19981217 <--
	MX 9911140	A	20000430	MX 1999-11140	19991202 <--
	US 6297228	B1	20011002	US 1999-445237	19991202 <--

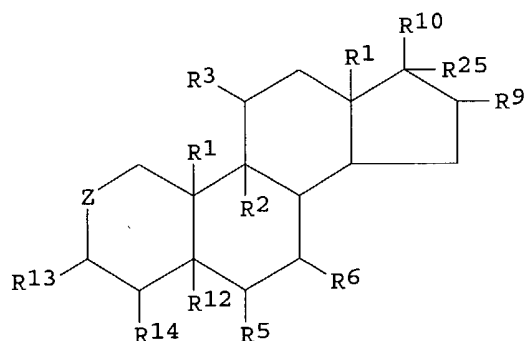
PRAI US 1991-796169	A	19911122	<--
US 1992-892448	A	19920602	<--
US 1992-941485	A	19920908	<--
US 1988-264918	A1	19881031	<--
US 1989-419226	B2	19891010	<--
US 1990-559123	B2	19900727	<--
WO 1992-US10133	A	19921123	<--
US 1994-342524	A1	19941121	<--
US 1997-895184	A	19970716	<--
WO 1998-US12711	W	19980618	<--

## CLASS

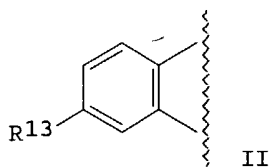
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9310141	ICM	C07J005-00
	ICS	A61K031-56; C07J003-00; C07J051-00; C07J011-00; C07J009-00; C07J041-00
US 5371078	ECLA	A61K031/56; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00 <--

OS MARPAT 119:160646

GI



I



II

AB Title compds. [I and II; R1 = H,  $\beta$ -Me,  $\beta$ -Et, R2 = H, F, Cl; R3 = H, alkoxy, alkanoyloxy, halo, O<sub>2</sub>CNH<sub>2</sub>, etc.; R2R3 = bond, O; R5 = H, OH, halo, Me, Ph, vinyl, alkyl, R6 = H, Me; R9 = H, OH, Me, F, 2-(alkoxy)ethyl, 2-(alkanoyloxy)ethyl, etc.; R10 = H, C.tplbond.CH, vinyl, halo, OH, Me, etc.; R12 = H; R1R12 = bond; R13 = H, OH, alkoxy, NH<sub>2</sub>, etc.; R14 = H; R12R14 = bond; R25 = OH, alkoxy, alkanoyloxy, CO<sub>2</sub>H, CH<sub>2</sub>OH, etc.; Z = CHR<sub>4</sub>, etc.; R4 = H, Me, Cl, F] were prepared Thus, tetrahydrocortisol-F was converted in 3 steps to 5 $\beta$ -pregnan-11 $\beta$ ,17 $\alpha$ ,21-triol-2-one. 4,9(11)-Pregnadiene-17 $\alpha$ ,21-diol-3,20-dione gave complete inhibition of lipopolysaccharide-induced corneal neovascularization in rabbit eye at 50  $\mu$ g in a pellet implant.

ST steroid prepn angiostatic; ocular hypertension treatment angiostatic steroid

IT Eye

(disease, neovascularization, treatment of, angiostatic steroids for)

IT Arteriosclerosis

Arthritis

Burn

Glaucoma (disease)

Granulation

Neoplasm



Shock  
Wound healing  
(prevention of neovascularization in, angiostatic steroids for)

IT Blood vessel, neoplasm  
(angiofibroma, prevention of neovascularization in, angiostatic steroids for)

IT Blood vessel, neoplasm  
(hemangioma, treatment of, angiostatic steroids for)

IT Blood vessel, disease  
(neovascularization, treatment of, angiostatic steroids for)

IT Injury  
(trauma, prevention of neovascularization in, angiostatic steroids for)

IT 57-63-6 68-23-5 68-60-0 302-97-6 566-35-8 633-29-4  
7753-60-8 10184-70-0  
RL: PROC (Process)  
(formulation of, as angiostatic agent)

IT 149916-71-2P 150213-49-3P 150213-50-6P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and reaction. of, in preparation of angiostatic agent)

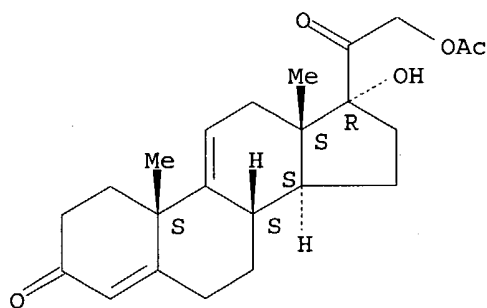
IT 641-84-9P 149916-54-1P 149916-55-2P 149916-56-3P 149916-57-4P  
149916-58-5P 149916-59-6P 149916-60-9P 149916-61-0P 149916-62-1P  
149916-63-2P 149916-64-3P 149916-65-4P 149916-66-5P 149916-67-6P  
149916-68-7P 149916-69-8P 149916-70-1P 149952-80-7P 149952-81-8P  
150213-68-6P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as angiostatic agent)

IT 53-02-1  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction. of, in preparation of angiostatic agent)

IT 7753-60-8 10184-70-0  
RL: PROC (Process)  
(formulation of, as angiostatic agent)

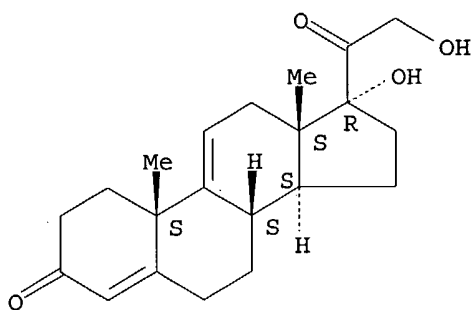
RN 7753-60-8 HCAPLUS  
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



RN 10184-70-0 HCAPLUS  
CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1992:152156 HCAPLUS  
 DN 116:152156  
 ED Entered STN: 17 Apr 1992  
 TI Preparation of 17a,21-dihydroxypregna-4,9(11)-diene-3,20-diones and  
 analogs as angiogenesis inhibitors  
 IN Wilks, John William; Dekoning, Thomas Frank; Aristoff, Paul Adrian  
 PA Upjohn Co., USA  
 SO PCT Int. Appl., 26 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07J031-00  
 ICS C07J009-00; C07J051-00; C07J007-00; C07J005-00; A61K031-56  
 ICA C07J003-00; C07J071-00  
 CC 32-5 (Steroids)  
 Section cross-reference(s): 1

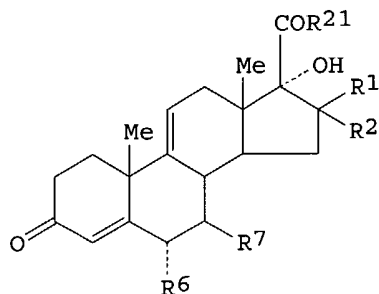
## FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9119731	A1	19911226	WO 1991-US3459	19910523 <--
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RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2081205	AA	19911212	CA 1991-2081205	19910523 <--
CA 2081205	C	20010227		
AU 9179848	A1	19920107	AU 1991-79848	19910523 <--
AU 657690	B2	19950323		
EP 533703	A1	19930331	EP 1991-910204	19910523 <--
EP 533703	B1	20000315		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05507912	T2	19931111	JP 1991-509678	19910523 <--
ES 2143978	T3	20000601	ES 1991-910204	19910523 <--
US 5972922	A	19991026	US 1995-575844	19951221 <--
HK 1013078	A1	20000929	HK 1998-114206	19981221 <--
GR 3033524	T3	20000929	GR 2000-401215	20000526 <--
PRAI US 1990-536894	A	19900611	<--	
US 1990-609661	A2	19901106	<--	
WO 1991-US3459	A	19910523	<--	
US 1994-178172	B1	19940106	<--	
US 1994-308061	B1	19940916	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9119731	ICM	C07J031-00
	ICS	C07J009-00; C07J051-00; C07J007-00; C07J005-00; A61K031-56

ICA C07J003-00; C07J071-00  
 OS MARPAT 116:152156  
 GI



I

- AB Title compds. [I; 1 of R1,R2 = H and the other = H or Me; R6 = H, F, Me; R7 = H, Me; R21 = CR213R214OR211, CR212R213SR211, CH2Br, etc.; R211 = H, P(O)(OH)2, COR212; R212 = alkyl; R213,R214 = H, alkyl] were prepared as angiogenesis inhibitors (no data). Thus, 17 $\alpha$ ,21-dihydroxypregna-4,9(11)-diene-3,20-dione 21-acetate was hydrolyzed to give 17 $\alpha$ ,21-dihydroxypregna-4,9(11)-diene-3,20-dione.
- ST pregnadienedione dihydroxy prepn angiogenesis inhibitor;  
 hydroxypregnadienedione prepn angiogenesis inhibitor
- IT Antidiabetics and Hypoglycemics  
 Neoplasm inhibitors  
 Parasitocides  
 (angiogenesis-inhibiting dihydroxypregnadienediones)
- IT Ovarian cycle  
 (disruption of, treatment of, angiogenesis-inhibiting dihydroxypregnadienediones for)
- IT Blood vessel  
 (formation of, inhibition of, dihydroxypregnadienediones and analogs for)
- IT Embryo  
 (implantation of, inhibition of, angiogenesis-inhibiting dihydroxypregnadienediones and analogs for)
- IT Burn  
**Glaucoma (disease)**  
 Psoriasis  
 (treatment of, angiogenesis-inhibiting dihydroxypregnadienediones for)
- IT Inflammation inhibitors  
 (antiarthritics, angiogenesis-inhibiting dihydroxypregnadienediones)
- IT Antiarteriosclerotics  
 (antiatherosclerotics, angiogenesis-inhibiting dihydroxypregnadienediones)
- IT **Eye, disease**  
 (neovascularization, prevention of, angiogenesis-inhibiting dihydroxypregnadienediones for)
- IT 133694-55-0P 133694-62-9P 133694-63-0P 133694-65-2P 139667-54-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and reaction of, in preparation of angiogenesis inhibitors)
- IT 378-61-0P 10184-69-7P **10184-70-0P** 19788-80-8P 50630-13-2P  
 88903-68-8P 103924-17-0P 111245-54-6P 133694-58-3P 133694-67-4P  
 139667-52-0P 139667-53-1P 139667-55-3P 139692-60-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as angiogenesis inhibitor)
- IT 1881-07-8 **7753-60-8** 105384-40-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, in preparation of angiogenesis inhibitors)

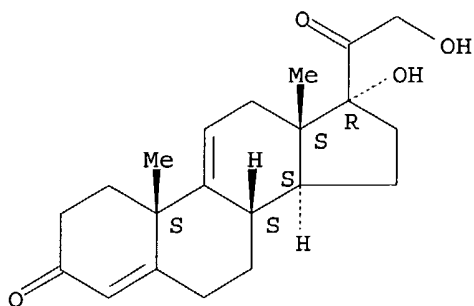
IT 10184-70-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as angiogenesis inhibitor)

RN 10184-70-0 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



IT 7753-60-8

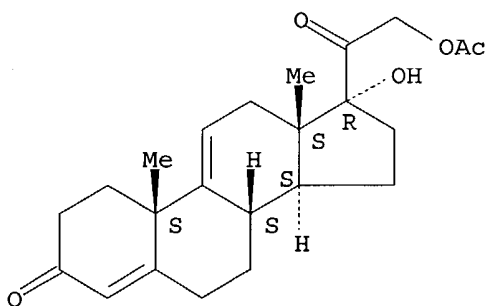
RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, in preparation of angiogenesis inhibitors)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1991:687178 HCAPLUS

DN 115:287178

ED Entered STN: 27 Dec 1991

TI Ophthalmic composition of angiostatic steroid-glucocorticoid combination  
for treatment of inflammation

IN Clark, Abbot F.

PA Alcon Laboratories, Inc., USA

SO PCT Int. Appl., 16 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-58

ICS A61K031-56

CC 63-6 (Pharmaceuticals)

FAN.CNT 7

PATENT NO.

KIND

DATE

APPLICATION NO.

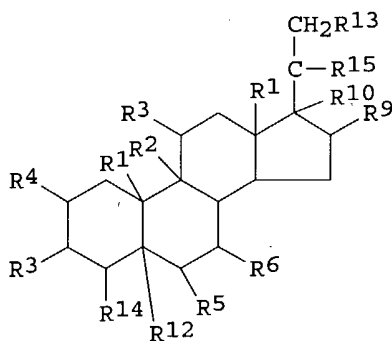
DATE

PI	WO 9103245	A1	19910321	WO 1990-US4071	19900725 <--
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	RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
	US 4945089	A	19900731	US 1989-399351	19890828 <--
	AU 9062952	A1	19910408	AU 1990-62952	19900725 <--
	AU 637824	B2	19930610		
	EP 489779	A1	19920617	EP 1990-912700	19900725 <--
	EP 489779	B1	19980128		
	R: AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, SE				
	JP 05500054	T2	19930114	JP 1990-512212	19900725 <--
	WO 9903503	A1	19990128	WO 1998-US12711	19980618 <--
	W: AU, BR, CA, JP, MX, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
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	AU 734195	B2	20010607		
	EP 1003553	A1	20000531	EP 1998-931367	19980618 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
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	JP 2001510170	T2	20010731	JP 2000-502798	19980618 <--
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PRAI	US 1989-399351	A	19890828	<--	
	US 1989-419226	A	19891010	<--	
	US 1987-139222	B1	19871229	<--	
	WO 1990-US4071	A	19900725	<--	
	US 1997-895184	A	19970716	<--	
	WO 1998-US12711	W	19980618	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9103245	ICM	A61K031-58
	ICS	A61K031-56

OS MARPAT 115:287178  
GI



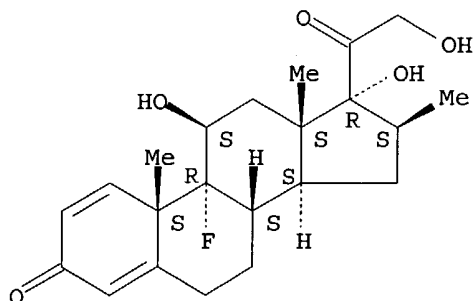
I

AB Pharmaceutical compns. useful in the treatment of ophthalmic inflammation, and methods of treating ophthalmic inflammation with those compns., are disclosed. The compns. contain a combination of a glucocorticoid and an angiostatic steroid, e.g. I [R1 =  $\beta$ -Me,  $\beta$ -Et; R2 = H, Cl; R3 = H, OH, alkoxy, etc., or R2R3 = O or double bond bridging C-9 and C-11, or R2 =  $\alpha$ -F and R3 =  $\beta$ -OH, or R2 =  $\alpha$ -Cl and R3 =  $\beta$ -Cl; R4 = H, Me, Cl, F; R5 = H, OH, F, Cl, Br, Me, Ph, vinyl, alkyl; R6 = H, Me; R9 = H, OH, Me, F, :CH<sub>2</sub>; R10 = H, OH, Me, or R10 forms a 2nd bond between C-16 and C-17; R12 = H or double bond with R14; R13 = H, OH, :O, OP(O)(OH)<sub>2</sub>, OC(O)(CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>H (n = 2-6); R14 = H, double bond with R12; R15

= :O, OH; R23 = OH, OPO(O)(OH)2, etc. (with provisions and exclusions)]. The angiostatic steroid substantially prevents any significant increases in intraocular pressure which might otherwise be experienced by the patient as a side effect of the glucocorticoid component of the compns. The therapeutic interaction of the 2 components therefore allows the potent anti-inflammatory properties of the glucocorticoids to be used without fear of elevating intraocular pressure. A formulation containing tetrahydrocortexolone and dexamethasone is given.

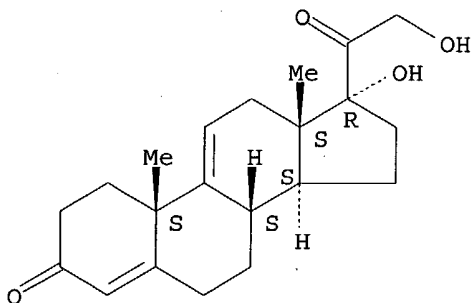
- ST glucocorticoid angiostatic steroid antiinflammatory ophthalmic;  
hydrocortexolone dexamethasone antiinflammatory ophthalmic
- IT Inflammation inhibitors  
(glucocorticoid-angiostatic steroid combinations, for ophthalmic pharmaceuticals)
- IT Steroids, compounds  
RL: BIOL (Biological study)  
(mixts. with glucocorticoids, angiostatic, for antiinflammatory ophthalmic pharmaceutical)
- IT Corticosteroids, compounds  
RL: BIOL (Biological study)  
(gluco-, mixts. with angiostatic steroid for antiinflammatory ophthalmic pharmaceutical)
- IT Pharmaceutical dosage forms  
(ophthalmic, of glucocorticoid and angiostatic steroid, for inflammation treatment)
- IT 50-02-2D, Dexamethasone, mixts. with angiostatic steroids 50-23-7D, Hydrocortisone, mixts. with angiostatic steroids 50-24-8D, Prednisolone, mixts. with angiostatic steroids 53-03-2D, Prednisone, mixts. with angiostatic steroids 68-60-0D, Tetrahydrocortexolone, mixts. with glucocorticoids 124-94-7D, Triamcinolone, mixts. with angiostatic steroids 378-44-9D, Betamethasone, mixts. with angiostatic steroids 426-13-1D, Fluorometholone, mixts. with angiostatic steroids 2668-66-8D, Medrysone, mixts. with angiostatic steroids 10184-70-0D, mixts. with glucocorticoids 105384-40-5D, mixts. with glucocorticoids 136305-04-9  
RL: BIOL (Biological study)  
(anti-inflammatory ophthalmic pharmaceuticals containing)
- IT 378-44-9D, Betamethasone, mixts. with angiostatic steroids 10184-70-0D, mixts. with glucocorticoids  
RL: BIOL (Biological study)  
(anti-inflammatory ophthalmic pharmaceuticals containing)
- RN 378-44-9 HCAPLUS
- CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11 $\beta$ ,16 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



- RN 10184-70-0 HCAPLUS
- CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1990:172351 HCAPLUS  
 DN 112:172351  
 ED Entered STN: 12 May 1990  
 TI Methods for controlling ocular hypertension with angiostatic steroids  
 IN Clark, Abbot F.  
 PA Alcon Laboratories, Inc., USA  
 SO U.S., 7 pp.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 IC ICM A61K031-56  
 ICS A61K031-58  
 NCL 514179000  
 CC 1-12 (Pharmacology)  
 FAN.CNT 7

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PI	US 4876250	A	19891024	US 1988-264918	19881031 <--
	AU 8943702	A1	19900503	AU 1989-43702	19891024 <--
	AU 628874	B2	19920924		
	CA 2001936	AA	19900430	CA 1989-2001936	19891031 <--
	CA 2001936	C	20000425		
	DK 8905429	A	19900501	DK 1989-5429	19891031 <--
	DK 172058	B1	19971006		
	EP 371617	A2	19900606	EP 1989-311238	19891031 <--
	EP 371617	A3	19920122		
	EP 371617	B1	19940608		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 02196722	A2	19900803	JP 1989-285990	19891031 <--
	JP 3049504	B2	20000605		
	AT 106731	E	19940615	AT 1989-311238	19891031 <--
	US 5371078	A	19941206	US 1992-941485	19920908 <--
	US 5407926	A	19950418	US 1992-966118	19921023 <--
	US 5698545	A	19971216	US 1996-643387	19960506 <--
	US 5990099	A	19991123	US 1997-994114	19971219 <--
	WO 9903503	A1	19990128	WO 1998-US12711	19980618 <--
	W: AU, BR, CA, JP, MX, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9881515	A1	19990210	AU 1998-81515	19980618 <--
	AU 734195	B2	20010607		
	EP 1003553	A1	20000531	EP 1998-931367	19980618 <--
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	BR 9811012	A	20001017	BR 1998-11012	19980618 <--
	JP 2001510170	T2	20010731	JP 2000-502798	19980618 <--

	MX 9911140	A	20000430	MX 1999-11140	19991202 <--
PRAI	US 1987-139222	B1	19871229	<--	
	US 1988-264918	A	19881031	<--	
	US 1989-399351	A2	19890828	<--	
	US 1989-419226	B2	19891010	<--	
	EP 1989-311238	A	19891031	<--	
	US 1990-555692	B1	19900723	<--	
	US 1990-559123	B2	19900727	<--	
	US 1992-941485	A1	19920908	<--	
	US 1994-349342	B1	19941202	<--	
	US 1996-643387	A1	19960506	<--	
	US 1997-895184	A	19970716	<--	
	US 1997-990424	B2	19971215	<--	
	WO 1998-US12711	W	19980618	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 4876250	ICM	A61K031-56
	ICS	A61K031-58
	NCL	514179000
US 5371078	ECLA	A61K031/56; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00 <--
US 5407926	ECLA	A61K031/565; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00 <--
US 5698545	ECLA	A61K031/565; A61K031/565; A61K031/565T10; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/57; A61K031/57L5; A61K031/58 <--
US 5990099	ECLA	A61K031/56; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00 <--

OS MARPAT 112:172351

AB Ocular hypertension including that associated with primary open angle glaucoma are treated topically with the steroids tetrahydrocortexolone (THS), 4,9(11)-pregnadiene-17 $\alpha$ ,21-diol-3,20-dione, 6 $\alpha$ -fluoro-17 $\alpha$ ,21-dihydroxy-16 $\beta$ -methylpregna-4,9(11)-diene-3,20-dione, and their pharmaceutically acceptable salts. These steroids may act by inhibiting the accumulation or stimulating the dissoln. of amorphous extracellular material in the trabecular meshwork of the eye. THS lowered intraocular pressure in rabbits with steroid-induced ocular hypertension.

ST eye hypertension treatment angiostatic steroid

IT **Glaucoma (disease)**

(angiostatic steroids for treatment of)

IT Steroids, biological studies

RL: BIOL (Biological study)

(angiostatic, in glaucoma treatment)

IT 68-60-0, Tetrahydrocortexolone 10184-70-0 105384-40-5

RL: BIOL (Biological study)

(glaucoma treatment with)

IT 10184-70-0

RL: BIOL (Biological study)

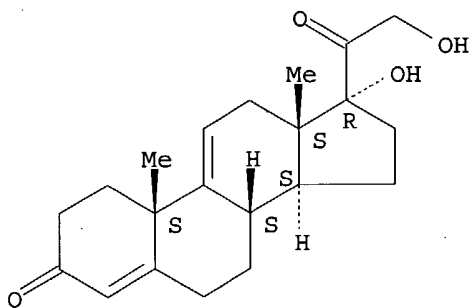
(glaucoma treatment with)

RN 10184-70-0 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.





L44 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1989:135568 HCAPLUS

DN 110:135568

ED Entered STN: 15 Apr 1989

TI Selective chlorination of steroids and other substrates directed by covalently linked agents comprising nitrogen-containing rings acting as templates

IN Breslow, Ronald; Brandl, Michael; Adam, Alan D.; Hunger, Jorgen

PA Columbia University, USA

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07J043-00

ICS C07J009-00; C07J001-00

CC 32-7 (Steroids)

Section cross-reference(s): 21

FAN.CNT 1

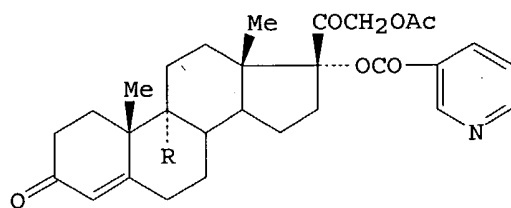
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8809337	A1	19881201	WO 1988-US1774	19880526 <--
	W: AU, DK, JP				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 4920216	A	19900424	US 1987-55139	19870528 <--
	AU 8819459	A1	19881221	AU 1988-19459	19880526 <--
PRAI	US 1987-55139		19870528	<--	
	WO 1988-US1774		19880526	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 8809337	ICM	C07J043-00
	ICS	C07J009-00; C07J001-00

OS CASREACT 110:135568; MARPAT 110:135568

GI



I

AB Hydroxy steroids were chlorinated at various ring H positions by esterifying with N-containing heterocyclic acids, which then act as templates

for regioselective chlorination by various agents. Esterification of cortexolone 21-acetate by nicotinic anhydride in MeOCH<sub>2</sub>CH<sub>2</sub>OMe containing 4-(dimethylamino)pyridine gave 97% of the 21-acetate 17 $\alpha$ -nicotinate I (R = H). This compound was chlorinated by 2.0 equiv SO<sub>2</sub>Cl<sub>2</sub> and 0.2 equiv AIBN in CH<sub>2</sub>Cl<sub>2</sub> under irradiation at 25° to give 100% crude I (R = Cl) containing approx. 10% I (R = H). Dehydrochlorination of I (R = Cl) using AgBF<sub>4</sub> in Me<sub>2</sub>CO gave the  $\Delta$ <sup>4</sup>,9(11) diene, 100% as crude and 70% after chromatog.

ST chlorination steroid nitrogen template; nicotinate cholestanol cortexolone template chlorination

IT Templates

(nitrogen-containing heterocyclic esters, for chlorination of hydroxy steroids and other compds.)

IT Dehydrogenation

(of steroids and other compds., via regioselective template chlorination and dehydrochlorination)

IT Dehydrochlorination

(regioselective template chlorination and, of steroids and other compds.)

IT Steroids, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

(regioselective template chlorination of, via nitrogen-containing heterocyclic esters)

IT Steroids, preparation

RL: SPN (Synthetic preparation); PREP (Preparation)

(chloro, preparation of, via regioselective template chlorination using nitrogen-containing heterocyclic esters)

IT Chlorination

(template, regioselective, of steroids and other compds., via esters with nitrogen-containing heterocyclic acids)

IT 7647-01-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(dehydrochlorination, regioselective template chlorination and, of steroids and other compds.)

IT 1333-74-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(dehydrogenation, of steroids and other compds., via regioselective template chlorination and dehydrochlorination)

IT 516-95-0, 3 $\alpha$ -Cholestanol

RL: RCT (Reactant); RACT (Reactant or reagent)

(esterification of, with carbonyldiimidazole)

IT 530-62-1

RL: RCT (Reactant); RACT (Reactant or reagent)

(esterification of, with cholestanol)

IT 16837-38-0, Nicotinic anhydride

RL: RCT (Reactant); RACT (Reactant or reagent)

(esterification of, with hydroxy steroids)

IT 640-87-9 24510-54-1

RL: RCT (Reactant); RACT (Reactant or reagent)

(esterification of, with nicotinic anhydride)

IT 108674-98-2P 119669-98-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and dehydrochlorination of)

IT 108665-15-2P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and dehydrochlorination, hydrolysis, and acetylation of)

IT 119669-94-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

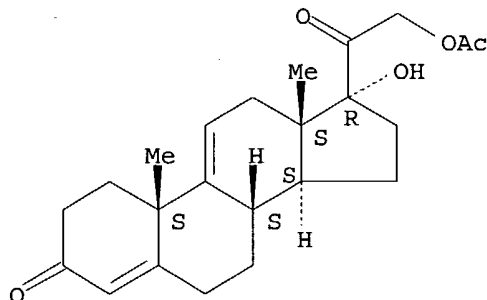
(preparation and hydrolysis and acetylation of)

IT 101836-12-8P 119669-90-8P 119669-91-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

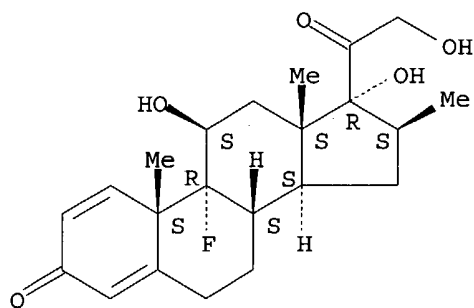
- (Reactant or reagent)  
(preparation and hydrolysis-dehydrochlorination of)
- IT 119669-99-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and methanolysis of)
- IT 108665-13-0P 119669-89-5P 119669-97-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and regioselective template chlorination of)
- IT 7753-60-8P 13209-41-1P 37772-32-0P 119669-92-0P  
119669-93-1P 119669-95-3P 119669-96-4P 119670-00-7P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, via regioselective template chlorination)
- IT 50-02-2DP, Dexamethasone, dehydro derivs. 50-24-8DP, dehydro derivs.  
124-94-7DP, Triamcinolone, dehydro derivs. 378-44-9DP, dehydro derivs.  
RL: PREP (Preparation)  
(production of, via regioselective template chlorination and dehydrochlorination)
- IT 932-72-9 7782-50-5, Chlorine, reactions 7791-25-5, Sulfuryl chloride  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(regioselective template chlorination by, of steroids and other organic compds.)
- IT 152-58-9 101836-11-7 108665-12-9 108665-14-1 119669-85-1  
119669-86-2 119669-87-3 119669-88-4  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(regioselective template chlorination of)
- IT 7753-60-8P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, via regioselective template chlorination)
- RN 7753-60-8 HCAPLUS
- CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



- IT 378-44-9DP, dehydro derivs.  
RL: PREP (Preparation)  
(production of, via regioselective template chlorination and dehydrochlorination)
- RN 378-44-9 HCAPLUS
- CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-,  
(11 $\beta$ ,16 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1984:190328 HCAPLUS  
 DN 100:190328  
 ED Entered STN: 08 Jun 1984  
 TI Conversion of 1,2-saturated 3-ketosteroids to 1,2-dehydrosteroids  
 IN Kominek, Leo Alyosius; Wolf, Holly Jo; Evans, Timothy Wendell  
 PA Upjohn Co., USA  
 SO Ger. Offen., 34 pp.  
 CODEN: GWXXBX  
 DT Patent  
 LA German  
 IC C07J007-00; C07J001-00; C07J005-00; C12P033-02  
 CC 16-2 (Fermentation and Bioindustrial Chemistry)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3322120	A1	19840202	DE 1983-3322120	19830620 <--
	DE 3322120	C2	19921008		
	US 4524134	A	19850618	US 1982-436552	19821025 <--
	HU 31767	O	19840528	HU 1983-2300	19830624 <--
	HU 196464	B	19881128		
	HU 196847	B	19890130	HU 1983-2671	19830624 <--
	GB 2123833	A1	19840208	GB 1983-17422	19830627 <--
	GB 2123833	B2	19860611		
	CH 657871	A	19860930	CH 1983-3784	19830708 <--
	DD 213242	A5	19840905	DD 1983-253123	19830715 <--
	NL 8302596	A	19840216	NL 1983-2596	19830720 <--
	JP 59039299	A2	19840303	JP 1983-134536	19830725 <--
	JP 06014874	B4	19940302		
	FR 2531101	A1	19840203	FR 1983-12564	19830729 <--
	FR 2531101	B1	19851115		
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	GB 2131811	B2	19860611		
	US 4704358	A	19871103	US 1985-721011	19850408 <--
	US 4684610	A	19870804	US 1985-724036	19850417 <--
	ES 549903	A3	19861201	ES 1985-549903	19851213 <--
	JP 06225792	A2	19940816	JP 1993-250926	19930914 <--
	JP 08024596	B4	19960313		
PRAI	US 1982-403949		19820730	<--	
	US 1982-436552		19821025	<--	
	US 1983-475437		19830315	<--	
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## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
DE 3322120	IC	C07J007-00IC C07J001-00IC C07J005-00IC C12P033-02

OS CASREACT 100:190328

AB Steroids are desatd. in the 1,2-position with dried cells of *Arthrobacter simplex* or *Bacterium cyclooxidans* in the presence of an exogenous electron carrier. Thus, 0.5 g of *B. cyclooxidans* ATCC 12673 cells that had been vacuum dried at 45° was added to 50 mL of 50 mM pH 7.5 phosphate buffer. Then 0.25 mL of an EtOH solution of menadione [58-27-5] (8.6 mg menadione/mL EtOH) was added and a 10% solution of 6 $\alpha$ -methylhydrocortisone (I) [1625-39-4] in DMF was added to a final concentration of 0.5 g/L. After shaking for 4 h at 28°, the transformation of I to 6 $\alpha$ -methylprednisolone [83-43-2] was 91%. The presence of a water-immiscible aromatic hydrocarbon increased the yield still more.

ST steroid desatn *Arthrobacter Bacterium*

IT Steroids, preparation  
RL: PREP (Preparation)  
(1,2-dehydro-3-keto, by microbial action)

IT *Arthrobacter simplex*  
*Bacterium cyclooxydans*  
(dried, steroid desatn. with)

IT Ubiquinones  
RL: BIOL (Biological study)  
(in steroid 1,2-desatn. with bacteria)

IT 50-23-7 63-05-8 382-44-5 382-45-6 433-82-9 434-03-7 564-33-0  
1035-69-4 1058-55-5 1176-81-4 1549-35-5 1625-39-4 2285-45-2  
2358-07-8 2395-17-7 2586-44-9 3386-04-7 3494-53-9 3932-49-8  
5327-59-3 **7753-60-8** 18762-16-8 18762-17-9 18769-18-1  
23460-76-6 24510-87-0 25092-31-3 34542-56-8 39780-54-6  
73553-82-9 74220-43-2 74915-67-6 85764-25-6 90039-83-1  
90039-84-2 90039-85-3 90039-86-4 90039-87-5 90039-88-6  
90081-44-0  
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)  
(1,2-desatn. of, bacterial)

IT 42613-28-5  
RL: BIOL (Biological study)  
(bacteria cells containing, steroid desatn. with)

IT 58-27-5 71-43-2, biological studies 108-88-3, biological studies  
130-15-4 130-36-9 299-11-6 956-48-9 1330-20-7, biological studies  
12001-79-5  
RL: BIOL (Biological study)  
(in steroid 1,2-desatn. with bacteria)

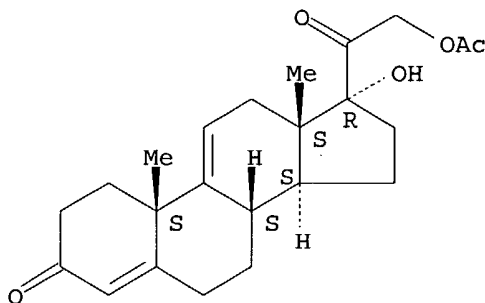
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356-12-7P **378-44-9P** 570-36-5P 806-29-1P 897-06-3P  
898-84-0P 910-99-6P 912-38-9P 981-34-0P 987-24-6P 1176-82-5P  
2476-74-6P 2597-76-4P 2823-42-9P 3859-65-2P 3870-07-3P  
3937-70-0P 4380-55-6P 6598-95-4P 7738-93-4P 7801-18-5P  
10106-41-9P 10184-69-7P 13209-41-1P 13504-15-9P 13889-22-0P  
15375-21-0P 18769-24-9P 25092-32-4P 37413-91-5P 39672-76-9P  
39780-55-7P 51166-61-1P 51259-83-7P 61919-52-6P 74410-22-3P  
77017-20-0P 83509-37-9P 90039-89-7P 90039-90-0P 90039-91-1P  
90039-92-2P 90039-93-3P 90039-94-4P 90039-95-5P 90039-96-6P  
90039-97-7P 90039-98-8P 90063-31-3P  
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)  
(manufacture of, microbial)

IT **7753-60-8**  
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)  
(1,2-desatn. of, bacterial)

RN **7753-60-8** HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



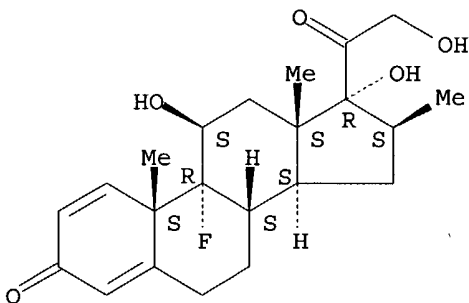
IT 378-44-9P

RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP  
(Preparation)  
(manufacture of, microbial)

RN 378-44-9 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-,  
(11β,16β) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> => d 140 all hitstr tot

L40 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:270085 HCAPLUS

DN 140:297513

ED Entered STN: 02 Apr 2004

TI Method using immunophilin-binding compounds for inhibiting choroidal  
neovascularization, animal model, and screening method

IN Laties, Alan; Wen, Rong; Lou, Zhijun

PA Trustees of the University of Pennsylvania, USA

SO PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N

CC 1-8 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004027027	A2	20040401	WO 2003-US29188	20030918
	WO 2004027027	A3	20040521		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,  
 GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,  
 LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,  
 OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,  
 TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,  
 NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
 GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-412088P P 20020918

# CLASS

PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

WO 2004027027 ICM C12N

- AB The invention discloses compns. and methods for inhibiting unwanted angiogenesis, particularly those of ocular tissues. The treatment, inhibition, and/or prevention of choroidal neovasculation (CNV) is provided, along with an animal model for CNV and imaging techniques that permit the screening of potential agents as anti-angiogenesis and anti-CNV agents. The methodol. of the invention uses immunophilin-binding compds., e.g. rapamycin.
- ST immunophilin binding compd choroidal neovascularization inhibition; drug screening animal model choroidal neovascularization
- IT Transcription factors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (NF- $\kappa$ B (nuclear factor of  $\kappa$  light chain gene enhancer in B-cells), inhibitors; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
- IT Eye, disease  
 (angioid streaks; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Integrins  
 Vitronectin receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (antagonists; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
- IT Metals, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (coordination; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
- IT Peptides, biological studies  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (cyclic; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
- IT Eye, disease  
 (diabetic retinopathy; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Angiogenesis inhibitors  
 Disease models  
 Drug delivery systems  
 Drug screening  
 Human  
 (immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Immunophilins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (immunophilin-binding compds. for inhibiting choroidal

- neovascularization, animal model, and screening method)
- IT Collagens, biological studies  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Drug targets  
Photosensitizers (pharmaceutical)  
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
- IT Antibodies and Immunoglobulins  
Interferons  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
- IT Vision  
(improvement; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Drug delivery systems  
(injections; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Dyes  
(lipophilic; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT **Eye, disease**  
(macula, degeneration; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT **Eye, disease**  
(macula, senile degeneration; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT **Eye, disease**  
(myopic degeneration; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Angiogenesis  
(neovascularization, retinal; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Eye, disease  
(ocular trauma; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Drug delivery systems  
(ophthalmic; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Drug delivery systems  
(oral; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Drug delivery systems  
(parenterals; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Ion channel blockers  
(potassium; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
- IT Histoplasma capsulatum  
(presumed ocular histoplasmosis syndrome; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)



- IT Eye, disease  
(retina, neovascularization; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Drug delivery systems  
(topical; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Blood vessel  
(visualization; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT Integrins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
( $\alpha\text{v}\beta 1$ , antagonists; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
- IT Integrins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
( $\alpha\text{v}\beta 3$ , antagonists; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
- IT Interferons  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
( $\gamma$ ; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
- IT 30525-89-4, Paraformaldehyde 119978-18-6, Matrigel  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT 53123-88-9, Rapamycin 53123-88-9D, Rapamycin, analogs 104987-11-3, Tacrolimus  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
- IT 64-86-8, Colchicine 124-94-7, Triamcinolone 145-63-1D, Suramin, analogs 154-42-7D, 6-Thioguanine, analogs 362-07-2, 2-Methoxyestradiol 989-51-5, Epigallocatechin-3-gallate 2295-31-0D, Thiazolidinedione, derivs. 4759-48-2, Accutane 6493-05-6, Pentoxifylline 7753-60-8, **Anecortave acetate** 9027-98-9, Arginine deiminase 15307-86-5, Diclofenac 16330-92-0 19171-19-8 23110-15-8, Fumagillin 25769-03-3, 1-Pyrrolidinecarbodithioic acid 78281-72-8, Nepafenac 82834-16-0, Perindopril 85441-61-8, Quinapril 86090-08-6, Angiostatin 97322-87-7, Troglitazone 122320-73-4, Rosiglitazone 127064-91-9, ANO 2 129298-91-5D, TNP 470, analogs 129497-78-5, Visudyne 145599-86-6, Cerivastatin 148717-90-2, Squalamine 162011-90-7, Rofecoxib 179324-69-7, Velcade 187888-07-9, Endostatin 197980-93-1, Pigment epithelium-derived factor 207692-22-6, AMG 1470 222716-86-1, Macugen 347396-82-1, Ranibizumab 675623-65-1, Endorepellin  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
- IT 9004-54-0, Dextran, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
- IT 9000-81-1, Acetylcholinesterase 9015-82-1, Angiotensin-converting enzyme

39391-18-9, Cyclooxygenase 140879-24-9, Proteasome 141436-78-4,  
Protein kinase C 148047-29-4, Tie-2 kinase 151769-13-0, Tiel receptor  
tyrosine kinase 171715-28-9, Mammalian target of rapamycin  
175449-82-8, Collagenase 3 386705-49-3, Vascular endothelial growth  
factor receptor kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; immunophilin-binding compds. for inhibiting choroidal  
neovascularization, animal model, screening method, and use with other  
agents)

IT 9028-02-8, Transfer RNA synthetase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(modulators; immunophilin-binding compds. for inhibiting choroidal  
neovascularization, animal model, screening method, and use with other  
agents)

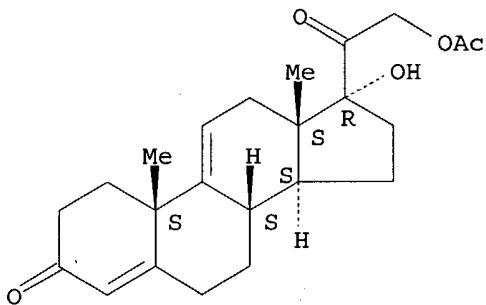
IT 7753-60-8, **Anecortave acetate**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(immunophilin-binding compds. for inhibiting choroidal  
neovascularization, animal model, screening method, and use with other  
agents)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:120728 HCAPLUS

DN 140:157931

ED Entered STN: 13 Feb 2004

TI Protection of visual acuity in patients with age related **macular  
degeneration** by administration of **anecortave  
acetate**

IN **Jerdan, Janice A.; Zilliox, Patricia; Robertson,  
Stella M.**

PA **Alcon, Inc., Switz.**

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-56

CC 2-4 (Mammalian Hormones)

Section cross-reference(s): 1

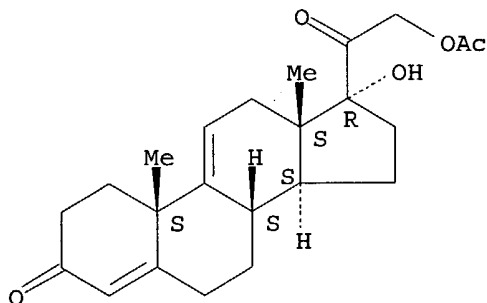
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004012742	A1	20040212	WO 2003-US20154	20030626 <--
	W: AU, BR, CA, CN, JP, KR, MX, PH, PL, RU, US, ZA				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,				

IT, LU, MC, NL, PT, RO, SE, SI, SK, TR  
 US 2004127472 A1 20040701 US 2003-606501 20030626 <--  
 PRAI US 2002-401220P P 20020805 <--  
 CLASS

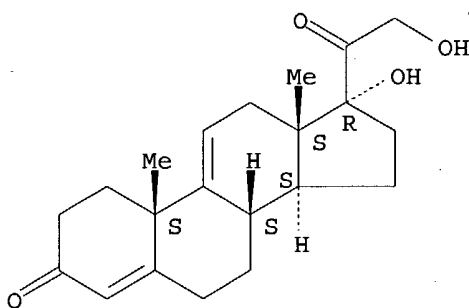
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004012742	ICM	A61K031-56
AB	The invention discloses the use of anecortave acetate or the alc. thereof for the protection of visual acuity in patients with age related <b>macular degeneration</b> .	
ST	<b>anecortave acetate</b> vision acuity age related <b>macular degeneration</b>	
IT	<b>Eye, disease</b> ( <b>macula, senile degeneration</b> ; protection of visual acuity in patients with age related <b>macular degeneration</b> by administration of <b>anecortave acetate</b> )	
IT	Drug delivery systems Human <b>Vision</b> (protection of visual acuity in patients with age related <b>macular degeneration</b> by administration of <b>anecortave acetate</b> )	
IT	<b>7753-60-8, Anecortave acetate</b> <b>10184-70-0</b> RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (protection of visual acuity in patients with age related <b>macular degeneration</b> by administration of <b>anecortave acetate</b> )	
IT	<b>7753-60-8, Anecortave acetate</b> <b>10184-70-0</b> RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (protection of visual acuity in patients with age related <b>macular degeneration</b> by administration of <b>anecortave acetate</b> )	
RN	<b>7753-60-8 HCAPLUS</b>	
CN	Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)	

Absolute stereochemistry.



RN 10184-70-0 HCAPLUS  
 CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:153653 HCAPLUS

DN 139:53197

ED Entered STN: 28 Feb 2003

TI **Anecortave acetate**: Treatment of age-related  
**macular degeneration** angiogenesis inhibitor

AU Sorbera, L. A.; Leeson, P. A.; Castaner, J.; Bayes, M.

CS Prous Science, Barcelona, 08080, Spain

SO Drugs of the Future (2002), 27(11), 1039-1048

CODEN: DRFUD4; ISSN: 0377-8282

PB Prous Science

DT Journal; General Review

LA English

CC 32-0 (Steroids)

Section cross-reference(s): 1

AB A review was presented of syntheses and pharmacol. of **anecortave acetate**. Angiogenesis is a normal process that is strictly controlled. If this fine control is disrupted, chronic activation can occur resulting in inappropriate tissue responses that can lead to pathol. neovascularization. Many chronic ocular diseases are due to chronic stimulation of angiogenesis and they are the major cause of blindness worldwide. Treatment for these ocular neovascular disorders should involve delay, arrest or prevention of new capillary proliferation with the absence of or the presence of only minimal adverse events. To date, surgery, laser photocoagulation and glucocorticoid therapy are the usual treatment options. However, they may be ineffective, worsen the condition or, in the case of glucocorticoids, be associated with steroid-induced adverse events. Several classes of antiangiogenic agents have been described and they include antibiotics, polypeptides, polycations, polyanions, steroids, VEGF antagonists and integrin antagonists. Angiostatic steroids in particular have been shown to inhibit angiogenesis without the typical steroid activity that is associated with side effects. One such novel angiostatic steroid chosen for further development is **anecortave acetate**. It has shown excellent preclin. antiangiogenic efficacy and promising clin. activity as a treatment for ocular neovascular disorders.

ST review **anecortave acetate** angiogenesis inhibitor  
neovascularization eye disease; **macular degeneration**  
angiogenesis inhibitor **anecortave acetate** review

IT **Eye, disease**

(**macula, senile degeneration, treatment**;  
review was presented of syntheses and pharmacol. of **anecortave acetate**, an age-related **macular degeneration**  
angiogenesis inhibitor)

IT Angiogenesis inhibitors

(review was presented of syntheses and pharmacol. of **anecortave acetate**, an age-related **macular degeneration**  
angiogenesis inhibitor)

IT 7753-60-8P, **Anecortave acetate**

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(review was presented of syntheses and pharmacol. of **anecortave acetate**, an age-related **macular degeneration** angiogenesis inhibitor)

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD

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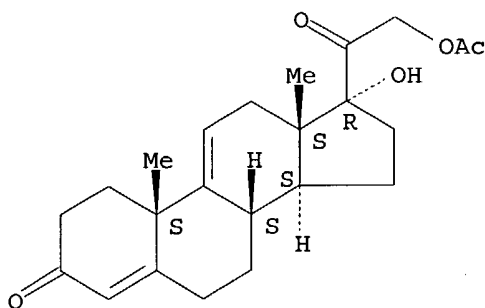
IT 7753-60-8P, **Anecortave acetate**

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(review was presented of syntheses and pharmacol. of **anecortave acetate**, an age-related **macular degeneration** angiogenesis inhibitor)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> => fil embase

FILE 'EMBASE' ENTERED AT 16:29:04 ON 01 SEP 2004  
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L59 ANSWER 1 OF 6 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN

AN 2003072455 EMBASE

TI **Anecortave acetate**: Treatment of age-related  
**macular degeneration** angiogenesis inhibitor.

AU Sobrera L.A.; Leeson P.A.; Castaner J.; Bayes M.

CS L.A. Sobrera, Prous Science, P.O. Box 540, 08080 Barcelona, Spain

SO Drugs of the Future, (1 Nov 2002) 27/11 (1039-1048).

Refs: 42

ISSN: 0377-8282 CODEN: DRFUD4

CY Spain

DT Journal; Article

FS 030 Pharmacology

037 Drug Literature Index

LA English

SL English

AB Angiogenesis is a normal process that is strictly controlled. If this fine control is disrupted, chronic activation can occur resulting in inappropriate tissue responses that can lead to pathologic neovascularization. Many chronic ocular diseases are due to chronic stimulation of angiogenesis and they are the major cause of blindness worldwide. Treatment for these ocular neovascular disorders should involve delay, arrest or prevention of new capillary proliferation with the absence of or the presence of only minimal adverse events. To date, surgery, laser photocoagulation and glucocorticoid therapy are the usual treatment options. However, they may be ineffective, worsen the condition or, in the case of glucocorticoids, be associated with steroid-induced adverse events. Several classes of antiangiogenic agents have been described and they include antibiotics, polypeptides, polycations, polyanions, steroids, VEGF antagonists and integrin antagonists. Angiostatic steroids in particular have been shown to inhibit angiogenesis without the typical steroid activity that is associated with side effects. One such novel angiostatic steroid chosen for further development is **anecortave acetate**. It has shown excellent preclinical antiangiogenic efficacy and promising clinical activity as a treatment for

ocular neovascular disorders.

CT Medical Descriptors:

- \*retina macula age related degeneration: DT, drug therapy
- \*retina macula age related degeneration: TH, therapy

laser coagulation

angiogenesis

- retina neovascularization: CO, complication
- retina neovascularization: DT, drug therapy
- retina neovascularization: TH, therapy
- blindness: CO, complication

corticosteroid therapy

drug efficacy

drug activity

drug synthesis

drug structure

drug mechanism

animal model

drug safety

article

Drug Descriptors:

- \*angiogenesis inhibitor: AN, drug analysis
- \*angiogenesis inhibitor: DV, drug development
- \*angiogenesis inhibitor: DT, drug therapy
- \*angiogenesis inhibitor: PD, pharmacology
- \*steroid: AN, drug analysis
- \*steroid: DV, drug development
- \*steroid: DT, drug therapy
- \*steroid: PD, pharmacology
- \*anecortave: AN, drug analysis
- \*anecortave: DV, drug development
- \*anecortave: DO, drug dose
- \*anecortave: DT, drug therapy
- \*anecortave: PD, pharmacology

antibiotic agent: DT, drug therapy

polypeptide: DT, drug therapy

polycation: DT, drug therapy

polyanion: DT, drug therapy

vasculotropin inhibitor: DT, drug therapy

integrin

integrin antagonist: DT, drug therapy

urokinase

stromelysin

plasminogen activator inhibitor 1

unclassified drug

RN (anecortave) 7753-60-8; (urokinase) 139639-24-0;  
(stromelysin) 79955-99-0; (plasminogen activator inhibitor 1) 140208-23-7

CN (1) A1 3789

CO (1) Alcon (United States)

L59 ANSWER 2 OF 6 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

AN 2003034758 EMBASE

TI New treatments for CNV secondary to AMD: What evidence exists to support a  
treatment recommendation?.

AU Lanzetta P.

CS P. Lanzetta, Department of Ophthalmology, University of Udine, Viale  
Venezia 410, 33100 Udine, Italy. paolo.lanzetta@dsc.uniud.it

SO Graefe's Archive for Clinical and Experimental Ophthalmology, (2002)  
240/11 (885-888).

Refs: 34

ISSN: 0721-832X CODEN: GACODL

CY Germany

DT Journal; Editorial

FS 012 Ophthalmology  
 017 Public Health, Social Medicine and Epidemiology  
 030 Pharmacology  
 036 Health Policy, Economics and Management  
 037 Drug Literature Index

LA English

CT Medical Descriptors:

- \*subretinal neovascularization: CO, complication
- \*subretinal neovascularization: DM, disease management
- \*subretinal neovascularization: DT, drug therapy
- \*subretinal neovascularization: RT, radiotherapy
- \*subretinal neovascularization: SU, surgery
- \*subretinal neovascularization: TH, therapy
- retina macula age related degeneration: DT, drug therapy
- eye disease: CO, complication
- eye disease: DM, disease management
- eye disease: DT, drug therapy
- eye disease: RT, radiotherapy
- eye disease: SU, surgery
- eye disease: TH, therapy
- visual impairment: CO, complication
- quality of life
- laser coagulation
- photodynamic therapy
- hyperthermic therapy
- retina macula translocation
- drug efficacy
- disease severity
- drug safety
- risk assessment
- visual acuity
- treatment outcome
- long term care
- gene therapy
- prognosis
- health care quality
- medical care
- patient care
- human
- clinical trial
- adult
- editorial
- priority journal

Drug Descriptors:

- angiogenesis inhibitor: CT, clinical trial
- angiogenesis inhibitor: DT, drug therapy
- angiogenesis inhibitor: PD, pharmacology
- benzoporphyrin derivative: CT, clinical trial
- benzoporphyrin derivative: DT, drug therapy
- benzoporphyrin derivative: PD, pharmacology
- antioxidant: CB, drug combination
- antioxidant: DT, drug therapy
- antioxidant: PO, oral drug administration
- zinc derivative: CB, drug combination
- zinc derivative: DT, drug therapy
- zinc derivative: PO, oral drug administration
- placebo
- tin ethyl etiopurpurin: CT, clinical trial
- tin ethyl etiopurpurin: DT, drug therapy
- tin ethyl etiopurpurin: PD, pharmacology
- photosensitizing agent: CT, clinical trial
- photosensitizing agent: DT, drug therapy
- photosensitizing agent: PD, pharmacology



indocyanine green  
 interferon: CT, clinical trial  
 interferon: DT, drug therapy  
 interferon: PD, pharmacology  
 matrix metalloproteinase inhibitor: CT, clinical trial  
 matrix metalloproteinase inhibitor: DT, drug therapy  
 matrix metalloproteinase inhibitor: PD, pharmacology  
 prinomastat: CT, clinical trial  
 prinomastat: DT, drug therapy  
 prinomastat: PD, pharmacology  
 vasculotropin inhibitor: CT, clinical trial  
 vasculotropin inhibitor: DT, drug therapy  
 vasculotropin inhibitor: PD, pharmacology  
 aptamer  
 rhufab v2: CT, clinical trial  
 rhufab v2: DT, drug therapy  
 vasculotropin antibody: CT, clinical trial  
 vasculotropin antibody: DT, drug therapy  
     **anecortave: CT, clinical trial**  
     **anecortave: DT, drug therapy**  
     **anecortave: PD, pharmacology**  
 steroid: CT, clinical trial  
 steroid: DT, drug therapy  
 steroid: PD, pharmacology  
 alpha tocopherol: CB, drug combination  
 alpha tocopherol: DT, drug therapy  
 alpha tocopherol: PO, oral drug administration  
 beta carotene: CB, drug combination  
 beta carotene: DT, drug therapy  
 beta carotene: PO, oral drug administration  
 zinc oxide: CB, drug combination  
 zinc oxide: DT, drug therapy  
 zinc oxide: PO, oral drug administration  
 cupric oxide: CB, drug combination  
 cupric oxide: DT, drug therapy  
 cupric oxide: PO, oral drug administration  
 copper derivative: CB, drug combination  
 copper derivative: DT, drug therapy  
 copper derivative: PO, oral drug administration  
 unclassified drug

RN (benzoporphyrin derivative) 113719-89-4; (indocyanine green) 3599-32-4;  
 (prinomastat) 192329-42-3, 195008-93-6; (**anecortave**)  
 7753-60-8; (alpha tocopherol) 1406-18-4, 1406-70-8, 52225-20-4,  
 58-95-7, 59-02-9; (beta carotene) 7235-40-7; (zinc oxide) 1314-13-2;  
 (cupric oxide) 1317-38-0  
 CN (1) Visudyne; Ag 3340  
 CO (1) Novartis

L59 ANSWER 3 OF 6 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 2001050805 EMBASE  
 TI IBC's 6th annual conference on angiogenesis: Novel therapeutic  
 developments.  
 AU Mousa S.A.  
 CS S.A. Mousa, DuPont Pharmaceuticals Co., Wilmington, DE, United States  
 SO Expert Opinion on Investigational Drugs, (2001) 10/2 (387-391).  
 ISSN: 1354-3784 CODEN: EOIDER  
 CY United Kingdom  
 DT Journal; Article  
 FS 005 General Pathology and Pathological Anatomy  
 012 Ophthalmology  
 014 Radiology  
 016 Cancer

037 Drug Literature Index  
038 Adverse Reactions Titles

LA English  
SL English

AB Angiogenesis is a process that is dependent upon co-ordinate production of angiogenesis stimulatory and inhibitory (angiostatic) molecules. Any imbalance in this regulatory circuit may lead to the development of a number of angiogenesis-mediated diseases. Angiogenesis is a multi-step process including activation, adhesion, migration, proliferation and transmigration of endothelial cells across cell matrices to or from new capillaries and from existing vessels. Angiogenesis is a process involved in the formation of new vessels by sprouting from pre-existing vessels. In contrast, vessel rudiments are sorted by a process termed vasculogenesis. Endothelial heterogeneity and organ specificity might contribute to differences in the response to different anti-angiogenic mechanisms (cultured EC versus microvascular EC isolated from different tissues). Under normal physiological conditions in mature organisms, endothelial cell turnover or angiogenesis is extremely slow (from months to years). However, angiogenesis can be activated for a limited time in certain situations such as wound healing and ovulation. In certain pathological states, such as human metastasis (oncology) and ocular neovascularisation, disorders including diabetic retinopathy and age-related **macular degeneration** (ophthalmology), there is excessive and sustained angiogenesis. Hence, understanding the mechanisms involved in the regulation of angiogenesis could have a major impact in the prevention and treatment of pathological angiogenic processes. Additionally, endothelial cells play a major role in the modelling of blood vessels. The interplay of growth factors, cell adhesion molecules, matrix proteases and specific signal transduction pathways either in the maintenance of the quiescent state or in the reactivation of endothelial cells is critical in physiological and pathological angiogenic processes.

CT Medical Descriptors:  
\*angiogenesis  
regulatory mechanism  
disease course  
endothelium cell  
cell activation  
cell adhesion  
cell migration  
cell proliferation  
cell transfer  
extracellular matrix  
capillary  
cell heterogeneity  
cell culture  
cell isolation  
tissue  
physiology  
turnover time  
wound healing  
ovulation  
pathology  
metastasis  
    **eye disease: DT, drug therapy**  
    **diabetic retinopathy**  
    **retina macula degeneration**  
ophthalmology  
model  
signal transduction  
cancer therapy  
protein domain  
solid tumor: DT, drug therapy  
side effect: SI, side effect

nuclear magnetic resonance imaging

human

nonhuman

rat

clinical trial

phase 1 clinical trial

phase 2 clinical trial

phase 3 clinical trial

controlled study

animal cell

article

Drug Descriptors:

\*angiogenesis inhibitor: PD, pharmacology

angiogenic factor

cell adhesion molecule: EC, endogenous compound

growth factor: EC, endogenous compound

proteinase: EC, endogenous compound

heparin: CT, clinical trial

heparin: PD, pharmacology

anticoagulant agent: PD, pharmacology

low molecular weight heparin: PD, pharmacology

tinzaparin: CT, clinical trial

tinzaparin: DT, drug therapy

tinzaparin: PR, pharmaceuticals

tinzaparin: PD, pharmacology

tissue factor pathway inhibitor: CT, clinical trial

tissue factor pathway inhibitor: PR, pharmaceuticals

tissue factor pathway inhibitor: PD, pharmacology

kininostatin: AN, drug analysis

kininostatin: PD, pharmacology

high molecular weight kininogen: AN, drug analysis

high molecular weight kininogen: PD, pharmacology

vitronectin: EC, endogenous compound

monoclonal antibody: DV, drug development

monoclonal antibody: PD, pharmacology

collagen type 4: PD, pharmacology

imc 1c 11: CT, clinical trial

imc 1c 11: DV, drug development

imc 1c 11: PD, pharmacology

vasculotropin receptor: EC, endogenous compound

vasculotropin: EC, endogenous compound

vasculotropin antibody: CT, clinical trial

vasculotropin antibody: DT, drug therapy

matrix metalloproteinase inhibitor: CT, clinical trial

matrix metalloproteinase inhibitor: DT, drug therapy

matrix metalloproteinase inhibitor: PD, pharmacology

matrix metalloproteinase inhibitor: PO, oral drug administration

2 methoxyestradiol: CT, clinical trial

2 methoxyestradiol: TO, drug toxicity

2 methoxyestradiol: PD, pharmacology

2 methoxyestradiol: PO, oral drug administration

integrin: EC, endogenous compound

**anecortave: AE, adverse drug reaction**

**anecortave: CT, clinical trial**

**anecortave: DT, drug therapy**

**anecortave: PD, pharmacology**

unclassified drug

RN (proteinase) 9001-92-7; (heparin) 37187-54-5, 8057-48-5, 8065-01-8,  
9005-48-5; (tissue factor pathway inhibitor) 116638-34-7; (high molecular  
weight kininogen) 97792-85-3; (vasculotropin) 127464-60-2; (2  
methoxyestradiol) 362-07-2; (**anecortave**) 7753-60-8

CN (1) Imc 1c 11; (2) **Al 3789**

CO (1) Imclone; (2) Alcon

L59 ANSWER 4 OF 6 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN  
AN 2001029006 EMBASE  
TI The effect of an angiostatic steroid on neovascularization in a rat model  
of retinopathy of prematurity.  
AU Penn J.S.; Rajaratnam V.S.; Collier R.J.; Clark A.F.  
CS J.S. Penn, Dept. of Ophthalmol. and Visual Sci., Vanderbilt Univ. School  
of Medicine, 8016 Medical Center East, 2115 21st Avenue South, Nashville,  
TN 37232-8808, United States. john.penn@mcmail.vanderbilt.edu  
SO Investigative Ophthalmology and Visual Science, (2001) 42/1 (283-290).  
Refs: 57  
ISSN: 0146-0404 CODEN: IOVSDA  
CY United States  
DT Journal; Article  
FS 012 Ophthalmology  
037 Drug Literature Index  
LA English  
SL English  
AB Purpose. The inhibition of angiogenesis by angiostatic steroids has been  
demonstrated in a variety of systems, including rabbit and rat cornea.  
There is considerable interest in the therapeutic potential of this class  
of compounds for angiogenic ocular conditions such as diabetic  
retinopathy, **macular degeneration**, and retinopathy of  
prematurity (ROP). This study was designed to test the capacity of an  
angiostatic steroid, **anecortave acetate**, to inhibit  
retinal neovascularization using a rat model of ROP and to investigate the  
mechanism of the effect. Methods. At birth, rats were placed in an  
atmosphere of varying oxygen that produces retinal neovascular changes  
that approximate human ROP. The rats then received intravitreal injections  
of either **anecortave acetate** or vehicle at varying  
times, and all were subsequently placed in room air. Retinas were assessed  
for plasminogen activator inhibitor (PAI)-1 mRNA level by RNase protection  
assay at 1, 2, and 3 days after injection and for normal and abnormal  
blood vessel growth 3 days later. Results. A significant reduction in the  
severity of abnormal retinal neovascularization was observed in the  
steroid-treated eyes compared with vehicle-injected eyes in ROP rats, yet  
the extent of normal total retinal vascular area was not significantly  
different. The drug had no effect on either retinal vascular area or  
neovascularization when tested in room air-raised control rats.  
Drug-injected eyes demonstrated a six- to ninefold increase in PAI-1 mRNA  
at 1 to 3 days after injection. Conclusions. This study represents the  
first therapeutic effect of an angiostatic steroid in an animal model of  
neovascular retinopathy. Additionally, the induction of PAI-1 indicates a  
mechanism of action for this class of compounds, and this is a novel  
finding in vivo. Because **anecortave acetate**  
significantly inhibited pathologic retinal angiogenesis in this model,  
while not significantly affecting normal intraretinal vessels, it holds  
therapeutic potential for a number of human ocular conditions in which  
angiogenesis plays a critical pathologic role.  
CT Medical Descriptors:  
\*retina neovascularization: DT, drug therapy  
\*retrolental fibroplasia: DT, drug therapy  
angiogenesis  
diabetic retinopathy: DT, drug therapy  
retina macula degeneration: DT, drug therapy  
drug mechanism  
drug structure  
nonhuman  
rat  
animal experiment  
animal model  
controlled study

animal tissue

article

priority journal

Drug Descriptors:

\*steroid: AN, drug analysis

\*steroid: DT, drug therapy

\*steroid: PD, pharmacology

\*steroid: VI, intravitreal drug administration

\*anecortave: AN, drug analysis

\*anecortave: DT, drug therapy

\*anecortave: PD, pharmacology

\*anecortave: VI, intravitreal drug administration

plasminogen activator inhibitor 1: EC, endogenous compound

unclassified drug

RN (anecortave) 7753-60-8; (plasminogen activator  
inhibitor 1) 140208-23-7

CO Alcon (United States)

L59 ANSWER 5 OF 6 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

AN 2000082438 EMBASE

TI New therapies for the treatment of age-related **macular  
degeneration**.

AU Sarrafizadeh R.; Trese M.T.

CS M.T. Trese, Department of Biomedical Sciences, Eye Research Institute,  
Oakland University, Rochester, MI, United States. mgjt46@aol.com

SO Expert Opinion on Therapeutic Patents, (2000) 10/3 (333-341).

Refs: 62

ISSN: 1354-3776 CODEN: EOTPEG

CY United Kingdom

DT Journal; General Review

FS 012 Ophthalmology

030 Pharmacology

037 Drug Literature Index

LA English

SL English

AB Age-related **macular degeneration** (ARMD) is a leading  
cause of legal blindness in older adults. The visual loss caused by ARMD  
can be devastating and many of the current treatment modalities are  
ineffective or only of moderate benefit in preventing the progression of  
the disease. Furthermore, few treatment options are available to patients  
with more advanced cases of ARMD. This review highlights some aspects of  
our current understanding of ARMD and discusses recent patent applications  
related to the treatment of this disease. In particular, agents that  
promote retinal pigment epithelium (RPE) cell proliferation and compounds  
with anti-oxidant properties that may prove useful in the treatment of  
non-neovascular ARMD will be discussed. In addition, we review  
photodynamic therapy and anti-angiogenic compounds that show potential  
promise in the treatment of the neovascular form of ARMD.

CT Medical Descriptors:

\*aging

\*retina macula degeneration: DT, drug therapy

\*retina macula degeneration: TH, therapy

blindness: DT, drug therapy

blindness: TH, therapy

cell proliferation

drug efficacy

patent

photodynamic therapy

pigment epithelium

visual impairment: DT, drug therapy

visual impairment: TH, therapy

human

nonhuman  
clinical trial  
review

## Drug Descriptors:

acetylcarnitine: DT, drug therapy  
alpha2a interferon: CT, clinical trial  
alpha2a interferon: DT, drug therapy  
**anecortave: DV, drug development**  
angiogenesis inhibitor: DT, drug therapy  
antioxidant: DT, drug therapy  
antisense oligonucleotide  
astaxanthin: DT, drug therapy  
benzoporphyrin derivative: CT, clinical trial  
benzoporphyrin derivative: DT, drug therapy  
beta interferon: DT, drug therapy  
beta interferon: PD, pharmacology  
probucol: DT, drug therapy  
steroid: DV, drug development  
tranilast: DV, drug development  
xanthophyll: CB, drug combination  
xanthophyll: DT, drug therapy  
zeaxanthin: CB, drug combination  
zeaxanthin: DT, drug therapy

RN (acetylcarnitine) 14992-62-2; (alpha2a interferon) 76543-88-9; (**anecortave**) 7753-60-8; (astaxanthin) 472-61-7;  
(benzoporphyrin derivative) 113719-89-4; (probucol) 23288-49-5;  
(tranilast) 53902-12-8; (xanthophyll) 127-40-2, 52842-48-5; (zeaxanthin) 144-68-3

CN (1) Verteporfin

CO (1) Ciba Geigy; Vyrex corporation; Howard foundation; Toray; Sigma Tau; Vogel; Pharmacyclics; Alcon; Kissei; Abbott

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on STN

AN 1999404647 EMBASE

TI Changing therapeutic paradigms for exudative age-related **macular degeneration**: Antiangiogenic agents and photodynamic therapy.

AU Ciulla T.A.; Danis R.P.; Criswell M.; Pratt L.M.

CS T.A. Ciulla, IN Univ. Macular Degeneration Clinic, Department of Ophthalmology, Indiana University School Medicine, 702 Rotary Circle, Indianapolis, IN 46260, United States. tciulla@iupui.edu

SO Expert Opinion on Investigational Drugs, (1999) 8/12 (2173-2182).

Refs: 98

ISSN: 1354-3784 CODEN: EOIDER

CY United Kingdom

DT Journal; General Review

FS 012 Ophthalmology

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

LA English

SL English

AB Age related **macular degeneration** (AMD) is the leading cause of irreversible visual loss in the United States. Overall, approximately 10-20% of patients with AMD exhibit the exudative form, which is responsible for most of the estimated 1.2 m cases of severe visual loss from AMD. Visual loss develops in the exudative form of AMD due to abnormal choroidal neovascular membranes (CNVM) that develop under the retina, leak serous fluid and blood, and ultimately cause a blinding disciform scar in, and under, the retina. Currently, the only well-studied and widely accepted method of treatment is laser photocoagulation of the CNVM. However, only a minority of patients with exudative AMD show well-demarcated 'classic' CNVM amenable to laser treatment, and at least

half of these patients suffer persistent or recurrent CNVM formation within two years. In addition, since the treatment itself causes a blinding central scotoma when the CNVM is located subfoveally, many clinicians do not treat subfoveal CNVM. With these treatment limitations, there has been a great deal of interest in alternative therapies for AMD, including anti-angiogenic agents and photodynamic therapy. Angiogenesis involves a complex interplay of cellular events involving a cascade of factors that are both inhibitory and stimulatory. Soluble growth factors have been the best-known cell modulating agents in ophthalmology, but there are a multitude of potential sites for inhibition of angiogenesis by pharmacological agents. With regard to photodynamic therapy, a photosensitizing and low power laser light is used to activate the dye within the CNVM to cause vascular occlusion by a photochemical reaction. Closure of the CNVM is achieved without severe collateral damage to the non-vascular tissues as occurs with laser photocoagulation.

CT Medical Descriptors:

- \*retina macula age related degeneration: DT, drug therapy
- \*retina macula age related degeneration: EP, epidemiology
- \*retina macula age related degeneration: ET, etiology
- \*retina macula age related degeneration: SU, surgery
- \*photodynamic therapy
  - visual impairment: DT, drug therapy
  - visual impairment: EP, epidemiology
  - subretinal neovascularization: DT, drug therapy
  - subretinal neovascularization: EP, epidemiology
- laser coagulation
  - central scotoma: CO, complication
- pathogenesis
- side effect: CO, complication
- steroid therapy
- drug clearance
- human
- oral drug administration
- intravenous drug administration
- topical drug administration
- intravitreal drug administration
- clinical trial
- review

Drug Descriptors:

- \*angiogenesis inhibitor: CT, clinical trial
- \*angiogenesis inhibitor: DT, drug therapy
- \*angiogenesis inhibitor: PD, pharmacology
- \*photosensitizing agent: DV, drug development
- \*photosensitizing agent: DT, drug therapy
- \*photosensitizing agent: PR, pharmaceuticals
- \*photosensitizing agent: PK, pharmacokinetics
- \*photosensitizing agent: PD, pharmacology
- growth factor: EC, endogenous compound
- antibody: DT, drug therapy
- antibody: PD, pharmacology
- vasculotropin: EC, endogenous compound
- matrix metalloproteinase inhibitor: CT, clinical trial
- matrix metalloproteinase inhibitor: DT, drug therapy
- alpha interferon: AE, adverse drug reaction
- alpha interferon: CT, clinical trial
- alpha interferon: DT, drug therapy
- alpha interferon: PD, pharmacology
- prednisone: DT, drug therapy
- steroid: DT, drug therapy
- triamcinolone acetonide: CT, clinical trial
- triamcinolone acetonide: DT, drug therapy
- anecortave acetate: DV, drug development
- thalidomide: CT, clinical trial

thalidomide: DV, drug development  
thalidomide: DT, drug therapy  
thalidomide: PD, pharmacology  
phthalocyanine derivative: DV, drug development  
rose bengal: DV, drug development  
aspartylchlorin e6: DV, drug development  
lutetium: CB, drug combination  
lutetium: DV, drug development  
etiopurpurin: DV, drug development  
benzoporphyrin derivative: CT, clinical trial  
benzoporphyrin derivative: DV, drug development  
benzoporphyrin derivative: DT, drug therapy  
benzoporphyrin derivative: PR, pharmaceuticals  
benzoporphyrin derivative: PK, pharmacokinetics  
RN (vasculotropin) 127464-60-2; (prednisone) 53-03-2; (triamcinolone  
acetonide) 76-25-5; (thalidomide) 50-35-1; (rose bengal) 11121-48-5,  
11139-83-6, 632-68-8; (aspartylchlorin e6) 110230-98-3; (lutetium)  
7439-94-3; (benzoporphyrin derivative) 113719-89-4

=> => fil medline

FILE 'MEDLINE' ENTERED AT 16:31:53 ON 01 SEP 2004

FILE LAST UPDATED: 31 AUG 2004 (20040831/UP). FILE COVERS 1951 TO DATE.

On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD  
for details. OLD MEDLINE now back to 1951.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the  
MeSH 2004 vocabulary. See <http://www.nlm.nih.gov/mesh/> and  
[http://www.nlm.nih.gov/pubs/techbull/nd03/nd03\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html) for a  
description of changes.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> d all 165

L65 ANSWER 1 OF 1 MEDLINE on STN  
AN 2001087920 MEDLINE  
DN PubMed ID: 11133880  
TI The effect of an angiostatic steroid on neovascularization in a rat model  
of retinopathy of prematurity.  
AU Penn J S; Rajaratnam V S; Collier R J; Clark A F  
CS Department of Ophthalmology and Visual Sciences, Vanderbilt University  
School of Medicine, Nashville, Tennessee 37232-8808, USA..  
john.penn@mcmail.vanderbilt.edu  
NC EY07533 (NEI)  
SO Investigative ophthalmology & visual science, (2001 Jan) 42 (1)  
283-90.  
Journal code: 7703701. ISSN: 0146-0404.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200101  
ED Entered STN: 20010322  
Last Updated on STN: 20010322  
Entered Medline: 20010118  
AB PURPOSE: The inhibition of angiogenesis by angiostatic steroids has been  
demonstrated in a variety of systems, including rabbit and rat cornea.  
There is considerable interest in the therapeutic potential of this class  
of compounds for angiogenic ocular conditions such as diabetic



retinopathy, **macular degeneration**, and retinopathy of prematurity (ROP). This study was designed to test the capacity of an angiostatic steroid, **anecortave acetate**, to inhibit retinal neovascularization using a rat model of ROP and to investigate the mechanism of the effect. METHODS: At birth, rats were placed in an atmosphere of varying oxygen that produces retinal neovascular changes that approximate human ROP. The rats then received intravitreal injections of either **anecortave acetate** or vehicle at varying times, and all were subsequently placed in room air. Retinas were assessed for plasminogen activator inhibitor (PAI)-1 mRNA level by RNase protection assay at 1, 2, and 3 days after injection and for normal and abnormal blood vessel growth 3 days later. RESULTS: A significant reduction in the severity of abnormal retinal neovascularization was observed in the steroid-treated eyes compared with vehicle-injected eyes in ROP rats, yet the extent of normal total retinal vascular area was not significantly different. The drug had no effect on either retinal vascular area or neovascularization when tested in room air-raised control rats. Drug-injected eyes demonstrated a six- to ninefold increase in PAI-1 mRNA at 1 to 3 days after injection. CONCLUSIONS: This study represents the first therapeutic effect of an angiostatic steroid in an animal model of neovascular retinopathy. Additionally, the induction of PAI-1 indicates a mechanism of action for this class of compounds, and this is a novel finding in vivo. Because **anecortave acetate** significantly inhibited pathologic retinal angiogenesis in this model, while not significantly affecting normal intraretinal vessels, it holds therapeutic potential for a number of human ocular conditions in which angiogenesis plays a critical pathologic role.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

\*Angiogenesis Inhibitors: TU, therapeutic use

Animals

Animals, Newborn

Blotting, Northern

Disease Models, Animal

Infant, Newborn

Injections

Nuclease Protection Assays

Plasminogen Activator Inhibitor 1: BI, biosynthesis

Plasminogen Activator Inhibitor 1: GE, genetics

\*Pregnadienediols: TU, therapeutic use

RNA Probes

RNA, Messenger: BI, biosynthesis

Random Allocation

Rats

Rats, Sprague-Dawley

Retinal Neovascularization: ME, metabolism

Retinal Neovascularization: PA, pathology

\*Retinal Neovascularization: PC, prevention & control

\*Retinopathy of Prematurity: DT, drug therapy

Retinopathy of Prematurity: ME, metabolism

Retinopathy of Prematurity: PA, pathology

Vitreous Body

CN 0 (Angiogenesis Inhibitors); 0 (Plasminogen Activator Inhibitor 1); 0 (Pregnadienediols); 0 (RNA Probes); 0 (RNA, Messenger); 0 (**anecortave acetate**)

=> => fil biosis

FILE 'BIOSIS' ENTERED AT 16:34:26 ON 01 SEP 2004

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FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT

FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 26 August 2004 (20040826/ED)

FILE RELOADED: 19 October 2003.

=> d 168 all tot

L68 ANSWER 1 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
AN 2003:219511 BIOSIS  
DN PREV200300219511  
TI **Anecortave acetate**. Treatment of age-related  
**macular degeneration**, angiogenesis inhibitor.  
AU Sorbera, L. A. [Reprint Author]; Leeson, P. A. [Reprint Author]; Castaner,  
J. [Reprint Author]; Bayes, M. [Reprint Author]  
CS Prous Science, 08080, P.O. Box 540, Barcelona, Spain  
SO Drugs of the Future, (November 2002) Vol. 27, No. 11, pp. 1039-1048.  
print.  
ISSN: 0377-8282.  
DT Article  
LA English  
ED Entered STN: 7 May 2003  
Last Updated on STN: 7 May 2003  
CC Cytology - Animal 02506  
Cytology - Human 02508  
Pathology - Therapy 12512  
Cardiovascular system - Physiology and biochemistry 14504  
Sense organs - Pathology 20006  
Nervous system - Pathology 20506  
Pharmacology - General 22002  
Pharmacology - Clinical pharmacology 22005  
Pharmacology - Cardiovascular system 22010  
Pharmacology - Sense organs, associated structures and functions 22031  
IT Major Concepts  
Methods and Techniques; Pharmacology  
IT Parts, Structures, & Systems of Organisms  
microvascular endothelial cell: circulatory system; umbilical vein  
endothelial cell: circulatory system  
IT Diseases  
age-related **macular degeneration**: eye disease, drug  
therapy  
**Macular Degeneration** (MeSH)  
IT Diseases  
blindness: eye disease, nervous system disease  
Blindness (MeSH)  
IT Chemicals & Biochemicals  
**anecortave acetate**: cardiovascular-drug,  
ophthalmic-drug, synthesis  
IT Methods & Equipment  
chemical synthesis: laboratory techniques; condensation: laboratory  
techniques  
IT Miscellaneous Descriptors  
angiogenesis: inhibition  
ORGN Classifier  
Galliformes 85536  
Super Taxa  
Aves; Vertebrata; Chordata; Animalia  
Organism Name  
chicken (common)  
Taxa Notes  
Animals, Birds, Chordates, Nonhuman Vertebrates, Vertebrates  
ORGN Classifier  
Hominidae 86215

Super Taxa  
 Primates; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 U937 cell line (cell line)  
 human (common)  
 Taxa Notes  
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates  
 ORGN Classifier  
 Leporidae 86040  
 Super Taxa  
 Lagomorpha; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 rabbit (common)  
 Taxa Notes  
 Animals, Chordates, Lagomorphs, Mammals, Nonhuman Vertebrates, Nonhuman  
 Mammals, Vertebrates  
 ORGN Classifier  
 Muridae 86375  
 Super Taxa  
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 rat (common)  
 Taxa Notes  
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,  
 Rodents, Vertebrates  
 RN 7753-60-8 (**anecortave acetate**)

L68 ANSWER 2 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
 AN 2003:175226 BIOSIS  
 DN PREV200300175226  
 TI Motion Ophthalmoscopy Macula (MOM).  
 AU Ciardella, A. P. [Reprint Author]; Hathiromani, S. [Reprint Author];  
 Orlock, D. [Reprint Author]; Borodoker, N. [Reprint Author]; Yannuzzi, L.  
 A. [Reprint Author]  
 CS Ophthalmology, Manhattan Eye, Ear and Throat Hospital, New York, NY, USA  
 SO ARVO Annual Meeting Abstract Search and Program Planner, (2002) Vol. 2002,  
 pp. Abstract No. 4340. cd-rom.  
 Meeting Info.: Annual Meeting of the Association For Research in Vision  
 and Ophthalmology. Fort Lauderdale, Florida, USA. May 05-10, 2002.  
 DT Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)  
 LA English  
 ED Entered STN: 9 Apr 2003  
 Last Updated on STN: 9 Apr 2003  
 AB Purpose: To describe a new technique for imaging pathologic changes over  
 time in the fundus: Motion Ophthalmoscopy of the **Macula** (MOM).  
 Clinical examples utilizing the fusion of separate digital images into a  
 sequential, clinical course will be presented. Methods: Commercially  
 available software was used to fuse in a movie sequential digital fundus  
 photographs. Results: Three movies demonstrating the clinical course of  
 three patients with **macular** disease. The first movie shows  
 spontaneous resolution of a submacular hemorrhage in a patient with  
 polypoidal choroidal vasculopathy, over 1-year follow-up. The second  
 movie illustrates the resolution of a serous-sanguineous neurosensory  
**macular** detachment in a patient with idiopathic perifoveal  
 telangiectasia, after treatment with a single intravitreal injection of  
**anecortave acetate**. The follow-up was 1 year. The  
 third movie shows the clinical course of a patient with retinal  
 angiomatous proliferation, a variant of age related **macular**  
**degeneration**, over 1-year period. Conclusion: MOM is a simple but  
 innovative way of showing the clinical course of a patient over time. It  
 is ideal for a web site presentation, as well as interactive presentation  
 to a group at meetings. It is also a very effective mean of education for

the patient itself.

CC General biology - Symposia, transactions and proceedings 00520  
 Pathology - Therapy 12512  
 Sense organs - Physiology and biochemistry 20004  
 Sense organs - Pathology 20006  
 Nervous system - Pathology 20506  
 Pharmacology - Clinical pharmacology 22005  
 Pharmacology - Sense organs, associated structures and functions 22031

IT Major Concepts  
 Methods and Techniques; Ophthalmology (Human Medicine, Medical Sciences)

IT Parts, Structures, & Systems of Organisms  
 fundus: sensory system

IT Diseases  
 age related **macular degeneration**: eye disease  
**Macular Degeneration** (MeSH)

IT Diseases  
 idiopathic perifoveal telangiectasia: eye disease

IT Diseases  
 macular disease: eye disease

IT Diseases  
 polypoidal choroidal vasculopathy: eye disease

IT Diseases  
 retinal angiomatous proliferation: eye disease

IT Diseases  
 serous-sanguineous neurosensory macular detachment: eye disease, nervous system disease

IT Diseases  
 submacular hemorrhage: eye disease

IT Chemicals & Biochemicals  
**anecortave acetate**: ophthalmic-drug, intravitreal administration

IT Methods & Equipment  
 motion ophthalmoscopy of the macula: clinical techniques, diagnostic techniques; sequential digital fundus photography: clinical techniques, diagnostic techniques

IT Miscellaneous Descriptors  
 clinical course; digital images; interactive presentation; pathologic changes; web site presentation

ORGN Classifier  
 Hominidae 86215  
 Super Taxa  
 Primates; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 human (common): patient  
 Taxa Notes  
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 7753-60-8 (**anecortave acetate**)

L68 ANSWER 3 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
 AN 2003:154979 BIOSIS  
 DN PREV200300154979  
 TI Sub-Tenon's Administration of the Angiostatic Agent **Anecortave Acetate** in AMD Patients with Subfoveal Choroidal Neovascularization (CNV) - the Clinical Outcome.  
 AU Slakter, J. S. [Reprint Author]; Singerman, L. J.; Yannuzzi, L. A.; Russell, S. R.; Hudson, H. L.; Jerdan, J.; Zilliox, P.; Robertson, S.; Anecortave Acetate Study Group  
 CS Vitreous Ret Mac Consult of NY, New York, NY, USA  
 SO ARVO Annual Meeting Abstract Search and Program Planner, (2002) Vol. 2002, pp. Abstract No. 2909. cd-rom.  
 Meeting Info.: Annual Meeting of the Association For Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. May 05-10, 2002.

DT Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 26 Mar 2003  
 Last Updated on STN: 26 Mar 2003

AB Purpose: To evaluate efficacy and safety of the angiostatic agent **anecortave acetate** for inhibition of subfoveal CNV lesion growth in AMD patients in two clinical studies. Changes in visual acuity and lesion characteristic are being evaluated as measures of efficacy. Methods: In both studies, a sterile suspension of **anecortave acetate** or placebo is administered as a sub-Tenon's retrobulbar injection via a specially designed cannula. The first study is a masked randomized evaluation of three **anecortave acetate** dosages versus placebo, with optional re-injection at 6-month intervals. The second masked randomized study evaluates **anecortave acetate** or placebo following initial Visudyne PDT. In this 6-month study, patients are randomized to a single injection of one of two dosages of **anecortave acetate** or to placebo. Patients with either predominantly classic or minimally classic subfoveal lesions are eligible for this study, which is evaluating the effect of **anecortave acetate** on visual acuity and post-PDT lesion changes. Results: Enrollment is complete in both studies with a total of 264 patients enrolled by 22 clinical sites in North America and the EU. In the first study, 128 patients have been enrolled and treated, with 78 of these patients receiving at least one additional injection. In the second study, 115 of the 136 enrolled and treated patients have completed the study and been exited. In both of these studies, digital fluorescein and indocyanine green angiograms are being evaluated by the Digital Angiography Reading Center (DARC), and lesion characteristics (lesion area, CNV area, classic CNV area) will be compared over time across treatment groups. Conclusion: Differences across treatment groups in both best-corrected logMAR visual acuity and angiographic lesion characteristics will be compared and discussed.

CC General biology - Symposia, transactions and proceedings 00520  
 Pathology - Therapy 12512  
 Sense organs - Pathology 20006  
 Pharmacology - General 22002  
 Pharmacology - Clinical pharmacology 22005  
 Pharmacology - Sense organs, associated structures and functions 22031

IT Major Concepts  
 Ophthalmology (Human Medicine, Medical Sciences); Pharmacology

IT Diseases  
 AMD: eye disease, age-related **macular degeneration**  
**Macular Degeneration** (MeSH)

IT Diseases  
 subfoveal choroidal neovascularization: eye disease  
 Choroidal Neovascularization (MeSH)

IT Chemicals & Biochemicals  
 Visudyne: photosensitizer drug; **anecortave acetate**:  
 ophthalmic-drug, angiostatic agent, efficacy, safety, sub-Tenon's  
 retrobulbar injection

IT Methods & Equipment  
 digital fluorescein angiography: clinical techniques, diagnostic  
 techniques; indocyanine green angiography: clinical techniques,  
 diagnostic techniques; photodynamic therapy: clinical techniques,  
 therapeutic and prophylactic techniques

IT Miscellaneous Descriptors  
 clinical outcome; visual acuity

ORGN Classifier  
 Hominidae 86215  
 Super Taxa  
 Primates; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name

human (common): patient

Taxa Notes

Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 129497-78-5 (Visudyne)  
7753-60-8 (**anecortave acetate**)

L68 ANSWER 4 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
AN 2003:142495 BIOSIS  
DN PREV200300142495  
TI **Anecortave Acetate** Administered Sub-Tenon's  
Retrobulbar with and without Visudyne PDT in Patients with Subfoveal  
Age-Related **Macular Degeneration** (AMD) - Clinical  
Safety Profile.  
AU D'Amico, D. J. [Reprint Author]; Duker, J.; Regillo, C.; Schneebaum, C.;  
Beasley, C.  
CS Harvard Medical School, MA Eye and Ear Infirmary, Boston, MA, USA  
SO ARVO Annual Meeting Abstract Search and Program Planner, (2002) Vol. 2002,  
pp. Abstract No. 569. cd-rom.  
Meeting Info.: Annual Meeting of the Association For Research in Vision  
and Ophthalmology. Fort Lauderdale, Florida, USA. May 05-10, 2002.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English  
ED Entered STN: 19 Mar 2003  
Last Updated on STN: 19 Mar 2003  
AB Purpose: Since 1998, the Independent Safety Committee has provided an  
independent medical expert review of safety information related to the two  
ongoing clinical trials evaluating the angiostatic agent  
**anecortave acetate** when administered as a sub-Tenon's  
retrobulbar bolus to patients with subfoveal AMD. This Committee is  
composed of three clinical retina specialists in addition to an internist  
and the Alcon Medical Monitor responsible for the safety oversight of  
these studies. Meetings of the Committee have included both telephone  
conferences and in-person meetings to periodically review the accumulating  
body of safety information. Methods: Safety information is derived from  
general physical examinations and dilated ophthalmic examinations of the  
patients in both trials including indocyanine green and/or fluorescein  
angiograms. Results: Enrollment has been completed for both of these  
studies. In study C-98-03, which evaluates **anecortave**  
**acetate** monotherapy, 128 patients have been enrolled and treated.  
In study C-00-07, which evaluates the effect of **anecortave**  
**acetate** following PDT treatment with Visudyne(TM), 136 patients  
have been enrolled and treated. During the most recent Safety Committee  
meeting, 400 safety events from C-98-03 and 180 safety events from C-00-07  
were reviewed and discussed. Based on their review of safety changes,  
there has been no request by the Committee to make any study design  
changes or to interrupt enrollment in either study. Conclusion: The  
Independent Safety Committee has reviewed the accumulating safety reports  
of all changes in patients enrolled in two clinical trials evaluating the  
effect of **anecortave acetate** on patients with  
subfoveal AMD. There have been no clinically significant safety issues  
identified by the Independent Safety Committee to date.  
CC General biology - Symposia, transactions and proceedings 00520  
Radiation biology - Radiation and isotope techniques 06504  
Pathology - Therapy 12512  
Cardiovascular system - Heart pathology 14506  
Cardiovascular system - Blood vessel pathology 14508  
Sense organs - Pathology 20006  
Pharmacology - General 22002  
Pharmacology - Clinical pharmacology 22005  
Pharmacology - Cardiovascular system 22010  
Pharmacology - Sense organs, associated structures and functions 22031  
IT Major Concepts

Cardiovascular Medicine (Human Medicine, Medical Sciences);  
 Ophthalmology (Human Medicine, Medical Sciences); Pharmacology;  
 Radiology (Medical Sciences)

IT Diseases  
 subfoveal age-related **macular degeneration**: eye  
 disease, vascular disease, drug therapy, radiotherapy

IT Chemicals & Biochemicals  
**anecortave acetate**: cardiovascular-drug,  
 ophthalmic-drug, angiostatic activity, safety, sub-tenon's retrobulbar  
 bolus; visudyne: ophthalmic-drug, radiosensitizer-drug

IT Methods & Equipment  
 PDT [photodynamic therapy]: clinical techniques, therapeutic and  
 prophylactic techniques; fluorescein angiogram: clinical techniques,  
 diagnostic techniques, imaging and microscopy techniques, laboratory  
 techniques, spectrum analysis techniques; indocyanine green angiogram:  
 clinical techniques, diagnostic techniques, imaging and microscopy  
 techniques, laboratory techniques

ORGN Classifier  
 Hominidae 86215  
 Super Taxa  
 Primates; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 human (common): patient  
 Taxa Notes  
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 7753-60-8 (**anecortave acetate**)  
 129497-78-5 (visudyne)

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 AN 2001:319945 BIOSIS  
 DN PREV200100319945  
 TI Sub-Tenon's retrobulbar **anecortave acetate** with and  
 without Visudyne PDT in patients with subfoveal age-related  
**macular degeneration** (AMD): A review of the emerging  
 clinical safety profile of this new experimental treatment.

AU D'Amico, D. J. [Reprint author]; Adamis, A. P. [Reprint author]; Duker,  
 J.; Regillo, C.; Schneebaum, C.; Beasley, C.  
 CS Harvard Medical School, MA Eye and Ear Infirmary, Boston, MA, USA  
 SO IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S232. print.  
 Meeting Info.: Annual Meeting of the Association for Research in Vision  
 and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.

DT Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)

LA English  
 ED Entered STN: 4 Jul 2001  
 Last Updated on STN: 19 Feb 2002

CC Pathology - Diagnostic 12504  
 General biology - Symposia, transactions and proceedings 00520  
 Biochemistry studies - General 10060  
 Pathology - Therapy 12512  
 Cardiovascular system - Blood vessel pathology 14508  
 Integumentary system - Pathology 18506  
 Sense organs - Physiology and biochemistry 20004  
 Sense organs - Pathology 20006  
 Pharmacology - General 22002  
 Pharmacology - Clinical pharmacology 22005  
 Pharmacology - Sense organs, associated structures and functions 22031  
 Toxicology - General and methods 22501  
 Toxicology - Pharmacology 22504

IT Major Concepts  
 Ophthalmology (Human Medicine, Medical Sciences); Methods and  
 Techniques; Pharmacology

IT Parts, Structures, & Systems of Organisms

conjunctiva: sensory system; eye: sensory system; fovea: sensory system; lens: sensory system; macula: sensory system; retina: sensory system

IT Diseases  
abnormal vision: eye disease, toxicity

IT Diseases  
cataract: eye disease, toxicity  
Cataract (MeSH)

IT Diseases  
decreased visual acuity: eye disease, toxicity

IT Diseases  
eye pain: eye disease, toxicity

IT Diseases  
ocular foreign body sensation: eye disease, toxicity, side effect

IT Diseases  
ocular hyperemia: eye disease, toxicity, side effect

IT Diseases  
ocular pruritus: eye disease, integumentary system disease, toxicity

IT Diseases  
ptosis: eye disease, toxicity

IT Diseases  
retinal hemorrhage: eye disease, toxicity, vascular disease  
Retinal Hemorrhage (MeSH)

IT Diseases  
subconjunctival hemorrhage: eye disease, toxicity, vascular disease  
Eye Hemorrhage (MeSH)

IT Diseases  
subfoveal age-related **macular degeneration**: eye disease, treatment

IT Diseases  
tearing: eye disease, toxicity

IT Chemicals & Biochemicals  
Visudyne: ophthalmic-drug, side effects, toxicity; **anecortave acetate**: ophthalmic-drug, clinical trial, efficacy, safety, sub-Tenon's retrobulbar administration, toxicity; fluorescein: diagnostic agent; indocyanine green: diagnostic agent

IT Methods & Equipment  
PDT [photodynamic therapy]: therapeutic method; fluorescein angiography: diagnostic method; indocyanine green angiography: diagnostic method

IT Miscellaneous Descriptors  
visual acuity; Meeting Abstract

ORGN Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
human: patient  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 129497-78-5 (Visudyne)  
7753-60-8 (**anecortave acetate**)  
2321-07-5 (fluorescein)  
3599-32-4 (indocyanine green)

L68 ANSWER 6 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
AN 2001:319941 BIOSIS  
DN PREV200100319941  
TI Sub-Tenon's retrobulbar **anecortave acetate** with and without Visudyne<sup>TM</sup> photodynamic therapy (PDT) in patients with subfoveal choroidal neovascularization (CNV) in age-related **macular degeneration** (AMD).  
AU Singerman, L. J. [Reprint author]; Yannuzzi, L. A.; Russell, S.; Hudson,



H. L.; Jerdan, J.; Anecortave Acetate Study Group  
 CS Retina Associates of Cleveland, Cleveland, OH, USA  
 SO IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S231. print.  
 Meeting Info.: Annual Meeting of the Association for Research in Vision  
 and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.  
 DT Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)  
 LA English  
 ED Entered STN: 4 Jul 2001  
 Last Updated on STN: 19 Feb 2002  
 CC Cardiovascular system - Heart pathology 14506  
 General biology - Symposia, transactions and proceedings 00520  
 Pathology - Therapy 12512  
 Cardiovascular system - Blood vessel pathology 14508  
 Sense organs - Physiology and biochemistry 20004  
 Sense organs - Pathology 20006  
 Pharmacology - General 22002  
 Pharmacology - Clinical pharmacology 22005  
 Pharmacology - Sense organs, associated structures and functions 22031  
 IT Major Concepts  
 Cardiovascular Medicine (Human Medicine, Medical Sciences);  
 Ophthalmology (Human Medicine, Medical Sciences); Methods and  
 Techniques; Pharmacology  
 IT Parts, Structures, & Systems of Organisms  
 choroid: sensory system; fovea: sensory system; macula: sensory system  
 IT Diseases  
 age-related **macular degeneration**: eye disease,  
 treatment  
**Macular Degeneration** (MeSH)  
 IT Diseases  
 subfoveal choroidal neovascularization: eye disease, vascular disease,  
 treatment  
 Choroidal Neovascularization (MeSH)  
 IT Chemicals & Biochemicals  
 Visudyne: ophthalmic-drug; **anecortave acetate**:  
 ophthalmic-drug, dosage, efficacy, sub-Tenon's retrobulbar  
 administration  
 IT Methods & Equipment  
 photodynamic therapy: therapeutic method  
 IT Miscellaneous Descriptors  
 visual acuity; Meeting Abstract  
 ORGN Classifier  
 Hominidae 86215  
 Super Taxa  
 Primates; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 human: patient  
 Taxa Notes  
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates  
 RN 129497-78-5 (Visudyne)  
 7753-60-8 (**anecortave acetate**)  
 L68 ANSWER 7 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
 AN 2001:317760 BIOSIS  
 DN PREV200100317760  
 TI Subtenons retrobulbar **anecortave acetate** with and  
 without Visudyne PDT in patients with subfoveal age-related  
**macular degeneration** (AMD): A Digital Angiography  
 Reading Center (DARC) review of baseline characteristics.  
 AU Slakter, J. S. [Reprint author]; Freund, K. B. [Reprint author]; Coleman,  
 H. [Reprint author]; Wheatley, M. [Reprint author]; Carvalho, C. [Reprint  
 author]; Negrao, S. [Reprint author]; Zilliox, P.  
 CS DARC, New York, NY, USA

SO IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S231. print.  
Meeting Info.: Annual Meeting of the Association for Research in Vision  
and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 4 Jul 2001  
Last Updated on STN: 19 Feb 2002

CC Blood - Blood and lymph studies 15002  
General biology - Symposia, transactions and proceedings 00520  
Biochemistry studies - General 10060  
Biochemistry studies - Lipids 10066  
Pathology - Diagnostic 12504  
Pathology - Therapy 12512  
Blood - Blood cell studies 15004  
Sense organs - Physiology and biochemistry 20004  
Sense organs - Pathology 20006  
Pharmacology - General 22002  
Pharmacology - Clinical pharmacology 22005  
Pharmacology - Sense organs, associated structures and functions 22031  
Toxicology - General and methods 22501  
Toxicology - Pharmacology 22504

IT Major Concepts  
Ophthalmology (Human Medicine, Medical Sciences); Methods and  
Techniques; Pharmacology

IT Parts, Structures, & Systems of Organisms  
blood: blood and lymphatics; fovea: sensory system; fundus: sensory  
system; macula: sensory system

IT Diseases  
subfoveal age-related **macular degeneration**: eye  
disease, characterization, treatment

IT Chemicals & Biochemicals  
Visudyne: ophthalmic-drug; **anecortave acetate**:  
ophthalmic-drug, clinical trial, efficacy, subtenon retrobulbar  
administration, toxicity; fluorescein: diagnostic agent; indocyanine  
green: diagnostic agent; lipid

IT Methods & Equipment  
PDT [photodynamic therapy]: therapeutic method; fluorescein  
angiography: diagnostic method; indocyanine green angiography:  
diagnostic method

IT Miscellaneous Descriptors  
Meeting Abstract; Digital Angiography Reading Center:  
company/organization

ORGN Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
human: patient  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 129497-78-5 (Visudyne)  
7753-60-8 (**anecortave acetate**)  
2321-07-5 (fluorescein)  
3599-32-4 (indocyanine green)

L68 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
AN 2001:78076 BIOSIS  
DN PREV200100078076  
TI The effect of an angiostatic steroid on neovascularization in a rat model  
of retinopathy of prematurity.  
AU Penn, John S. [Reprint author]; Rajaratnam, Veeraramani S.; Collier,  
Robert J.; Clark, Abbot F.

CS Department of Ophthalmology and Visual Sciences, Vanderbilt University  
School of Medicine, 2115 21st Avenue South, 8016 Medical Center East,  
Nashville, TN, 37232-8808, USA  
john.penn@mcmail.vanderbilt.edu

SO IOVS, (January, 2001) Vol. 42, No. 1, pp. 283-290. print.

DT Article

LA English

ED Entered STN: 7 Feb 2001  
Last Updated on STN: 12 Feb 2002

AB Purpose. The inhibition of angiogenesis by angiostatic steroids has been demonstrated in a variety of systems, including rabbit and rat cornea. There is considerable interest in the therapeutic potential of this class of compounds for angiogenic ocular conditions such as diabetic retinopathy, **macular degeneration**, and retinopathy of prematurity (ROP). This study was designed to test the capacity of an angiostatic steroid, **anecortave acetate**, to inhibit retinal neovascularization using a rat model of ROP and to investigate the mechanism of the effect. Methods. At birth, rats were placed in an atmosphere of varying oxygen that produces retinal neovascular changes that approximate human ROP. The rats then received intravitreal injections of either **anecortave acetate** or vehicle at varying times, and all were subsequently placed in room air. Retinas were assessed for plasminogen activator inhibitor (PAI)-1 mRNA level by RNase protection assay at 1, 2, and 3 days after injection and for normal and abnormal blood vessel growth 3 days later. Results. A significant reduction in the severity of abnormal retinal neovascularization was observed in the steroid-treated eyes compared with vehicle-injected eyes in ROP rats, yet the extent of normal total retinal vascular area was not significantly different. The drug had no effect on either retinal vascular area or neovascularization when tested in room air-raised control rats. Drug-injected eyes demonstrated a six- to ninefold increase in PAI-1 mRNA at 1 to 3 days after injection. Conclusions. This study represents the first therapeutic effect of an angiostatic steroid in an animal model of neovascular retinopathy. Additionally, the induction of PAI-1 indicates a mechanism of action for this class of compounds, and this is a novel finding in vivo. Because **anecortave acetate** significantly inhibited pathologic retinal angiogenesis in this model, while not significantly affecting normal intraretinal vessels, it holds therapeutic potential for a number of human ocular conditions in which angiogenesis plays a critical pathologic role.

CC Pharmacology - Sense organs, associated structures and functions 22031  
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062  
Pathology - Therapy 12512  
Sense organs - Physiology and biochemistry 20004  
Sense organs - Pathology 20006  
Pharmacology - General 22002

IT Major Concepts  
Pharmacology; Sense Organs (Sensory Reception)

IT Parts, Structures, & Systems of Organisms  
retina: sensory system

IT Diseases  
retinopathy of prematurity: eye disease, treatment  
Retinopathy of Prematurity (MeSH)

IT Chemicals & Biochemicals  
**anecortave acetate** [4,9(11)-pregnadien-17-alpha,21-diol-3,20-dione-21-acetate]: ophthalmic-drug, angiostatic steroid, structure, usefulness; plasminogen activator inhibitor-1 messenger RNA: induction

IT Methods & Equipment  
RNase protection assay: analytical method

IT Miscellaneous Descriptors  
retinal neovascularization: inhibition

ORGN Classifier

Muridae 86375  
 Super Taxa  
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 rat: animal model, strain-Sprague-Dawley  
 Taxa Notes  
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,  
 Rodents, Vertebrates  
 RN 7753-60-8 (anecortave acetate)  
 7753-60-8 (4,9(11)-pregnadien-17-alpha,21-diol-3,20-dione-21-  
 acetate)

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L75 ANSWER 1 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2004-315778 [29] WPIX

DNC C2004-119770

TI Treatment, prevention and inhibition of angiogenesis-mediated diseases or  
 conditions of retina or choroid comprises administration of a composition  
 comprising an immunophilin binding active agent e.g. rapamycin.

DC B05

IN LATIES, A; LOU, Z; WEN, R

PA (UYPE-N) UNIV PENNSYLVANIA

CYC 105

PI WO 2004027027 A2 20040401 (200429)\* EN 27 C12N000-00

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS

LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP

KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG

PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC

VN YU ZA ZM ZW

ADT WO 2004027027 A2 WO 2003-US29188 20030918

PRAI US 2002-412088P 20020918

IC ICM C12N000-00

AB WO2004027027 A UPAB: 20040505

NOVELTY - Treatment, prevention and inhibition of angiogenesis-mediated diseases or conditions of the retina or choroid in a mammal comprises the administration of a composition (I) comprising an immunophilin binding active agent.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a composition comprising rapamycin, a rapamycin analog or tacrolimus and a carrier suitable for administration to the eye or eye tissue.

ACTIVITY - Antiangiogenic; Antidiabetic; Ophthalmological; Vasotropic.

The inhibition of choroidal neovasculation by rapamycin was tested in Sprague-Dawley rats. The results showed that rapamycin demonstrated a remarkable ability to inhibit new blood vessel formation.

MECHANISM OF ACTION - None given.

USE - (I) is useful for the treatment, prevention and inhibition of angiogenesis-mediated diseases or conditions (diabetic retinopathy, **macular degeneration** or preferably choroidal neovascularization (occurs in retinal or subretinal disorders of age-related **macular degeneration**, presumed ocular histoplasmosis syndrome, myopic **degeneration**, angioid streaks or ocular trauma) or (exudative) age-related **macular degeneration**) of the retina or choroid in a mammal. (I) is also useful in improving the ocular vision in retinal disorders characterized by choroidal neovascularization or angiogenesis of the retina of eye of the mammal (all claimed).

Dwg.0/3

FS CPI

FA AB; DCN

MC CPI: B01-A02; B01-B02; B01-C06; B01-D02; B02-R; B02-T; B03-A; B04-A06; B04-B03C; B04-C01; B04-H05; B04-N04; B05-A03B; B05-C06; B06-A01; B06-D01; B06-D03; B06-D18; B06-E05; B07-A01; B07-A03; B07-D03; B07-D04C; B07-D10; B07-F01; B10-A09B; B10-A12A; B10-B01B; B10-B02A; B14-D05C; B14-D06; B14-F02F2; B14-J02B1; B14-L01; B14-L06; B14-N03; B14-S04

TECH UPTX: 20040505

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: (I) is preferably rapamycin, its analog or tacrolimus. (I) is also administered with another agent (II) for the treatment of angiogenesis or neovascularization (particularly choroidal neovasculation (CNV)). (II) is preferably pyrrolidine, dithiocarbamate (nuclear factor kappa B kinase inhibitor), squalamine, TPN 470 analogue and fumagillin, protein kinase C inhibitors, Tie(tyrosine kinase inhibitor)-1 and Tie-2 kinase inhibitors, inhibitors of vascular endothelial growth factor (VEGF) receptor kinase, proteasome inhibitors such as Velcade (bortezomib), bortezomib, for injection, ranibizumab (Lucentis(ranibizumab) and other antibodies directed to the same target, pegaptanib (Macugen (pegaptanin sodium), vitronectin receptor antagonists, such as cyclic peptide antagonists of vitronectin receptor-type integrins, a-(vaso active intestinal peptide)VIP-3 integrin antagonists, a-VIP-1 integrin antagonists, thiazolidinediones such as rosiglitazone or troglitazone, interferon, including y-interferon or interferon targeted to CNV by use of dextran and metal coordination, pigment epithelium derived factor, endostatin, angiostatin, **anecortave acetate**, acetamide, triamcinolone, tetrathiomolybdate, Accutane (isotretinoin) (13-cis retinoic acid), ACE inhibitors such as quinopril or perindonil, inhibitors of mammalian target of rapamycin, 3-aminothalidomide, pentoxifylline, 2-methoxyestradiol, colchicines, AGM-1470, cyclooxygenase inhibitors such as nepafenac, rofecoxib, and diclofenac, t-RNA synthase modulator, metalloprotease 13 inhibitor, acetylcholinesterase inhibitor, potassium channel blockers, endorepellin, arginine deiminase, epigallocatechin-3-gallate, cerivastatin, analogues of suramin, and Visudyne.

ABEX UPTX: 20040505

ADMINISTRATION - Administration of (I) is intraocular, subretinal,

subcleral, intrachoroidal, subconjunctival, topical, oral or parenteral (claimed), at a dosage of 0.1-300 (preferably 1-10) mg/kg/day.

L75 ANSWER 2 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN  
 AN 2004-203578 [19] WPIX  
 DNC C2004-080256  
 TI Use of **anecortave acetate** to maintain or prevent the loss of visual acuity and inhibit lesion growth associated with age related **macular degeneration**.  
 DC B01  
 IN JERDAN, J A; ROBERTSON, S M; ZILLIOX, P  
 PA (JERD-I) JERDAN J A; (ROBE-I) ROBERTSON S M; (ZILL-I) ZILLIOX P; (ALCO-N) ALCON INC  
 CYC 38  
 PI WO 2004012742 A1 20040212 (200419)\* EN 29 A61K031-56  
 RW: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO  
 SE SI SK TR  
 W: AU BR CA CN JP KR MX PH PL RU US ZA  
 US 2004127472 A1 20040701 (200444) A61K031-56  
 AU 2003281817 A1 20040223 (200453) A61K031-56  
 ADT WO 2004012742 A1 WO 2003-US20154 20030626; US 2004127472 A1 Provisional US 2002-401220P 20020805, US 2003-606501 20030626; AU 2003281817 A1 AU 2003-281817 20030626  
 FDT AU 2003281817 A1 Based on WO 2004012742  
 PRAI US 2002-401220P 20020805; US 2003-606501 20030626  
 IC ICM A61K031-56  
 AB WO2004012742 A UPAB: 20040525  
 NOVELTY - Prevention of the loss of visual acuity, maintenance of visual acuity and inhibition of lesion growth associated with age related **macular degeneration** comprises juxtascleral administration of **anecortave acetate** (I) or its alcohol.  
 ACTIVITY - Ophthalmological.  
 MECHANISM OF ACTION - Protease inhibitor; Angiogenesis inhibitor; Urokinase-like plasminogen activator inhibitor; matrix metalloproteinase-3 inhibitor.  
 USE - (I) is useful for the preparation of a medicament for maintaining visual acuity, prevention of the loss of visual acuity and for the inhibition of lesion growth associated with age related **macular degeneration** (claimed).  
 (I) was analysed for severe vision loss at 6 month by comparing with baseline among treatment groups. The result showed that at 15 mg, (I) was 96.97% of less than 6 lines worse when compared to placebo treatment 76.67%.  
 ADVANTAGE - (I) is safe and does not produce glucocorticoid receptor-mediated steroidal side effects.  
 Dwg.0/5  
 FS CPI  
 FA AB; DCN  
 MC CPI: B01-C03; B01-C05; B14-C03  
 ABEX UPTX: 20040525  
 ADMINISTRATION - Administration of (I) is 3-30 (preferably 15) mg as a juxtascleral depot or juxtascleral implant (claimed).

L75 ANSWER 3 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN  
 AN 2002-672690 [72] WPIX  
 CR 2001-425112 [45]; 2001-432457 [46]; 2004-051015 [05]  
 DNN N2002-531711 DNC C2002-189451  
 TI Ophthalmic drug delivery device for clinical studies, incl comprising 4,9 (11)-pregnadien-17alpha,21-diol-3,20-dione, 4,9(11)-pregnadien-17alpha,21-diol-3,20-dione-21-acetate.  
 DC B01 B07 P32  
 IN YAACOBI, Y

*This is your compound - see pages 82-84*

PA (ALCO-N) ALCON UNIVERSAL LTD  
CYC 1  
PI US 6413540 B1 20020702 (200272)\* 13 A61F002-00  
ADT US 6413540 B1 Provisional US 1999-160673P 19991021, US 2000-660000  
20000912  
PRAI US 1999-160673P 19991021; US 2000-660000 20000912  
IC ICM A61F002-00  
AB US 6413540 B UPAB: 20040120  
NOVELTY - Ophthalmic drug delivery device comprises a body having a scleral surface for placement proximate a sclera and a well having an opening to the scleral surface, and an inner core in the well. The inner core comprises 4,9 (11)-pregnadien-17 alpha ,21-diol-3,20-dione, 4,9(11)-pregnadien-17 alpha ,21-diol-3,20-dione-21-acetate or eliprodil.  
USE - Used in clinical studies for localized delivery of active agent to the human eye having era, choroid and retina, Tenon's capsule and **macula**. In ophthalmic drug delivery, the device is especially useful for localized delivery of pharmaceutically active agents to the posterior segment of a eye to combat age related **macular degeneration** and choroidal neovascularization, retinopathies, retinitis, uveitis, **macular** edema and glaucoma.  
ADVANTAGE - The device is safe, effective, rate-controlled, and suitable for localized delivery of active agents to any body tissue. The surgical procedure for implanting the device is safe, simple, quick and capable of being performed in an outpatient setting. The device is easy and economical to manufacture.  
Dwg.0/7  
FS CPI GMPI  
FA AB; DCN  
MC CPI: B01-C06; B07-D05; B14-N03  
TECH UPTX: 20021108  
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Device: The body comprises a biocompatible, non-bioerodable material. The inner core is a tablet, comprising a hydrogel. The active agent is positioned within the hydrogel.

L75 ANSWER 4 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN  
AN 2001-451774 [48] WPIX  
DNN N2001-334447 DNC C2001-136453  
TI Plaque for intravitreal administration for treating intraocular conditions such as retinopathies, comprises inner and outer surfaces, and one or more guide units for guiding needle into interior portion of eye.  
DC B07 P32  
IN BILLSON, F A; GILLIES, M C; PENFOLD, P L  
PA (UNSY) UNIV SYDNEY; (BILL-I) BILLSON F A; (GILL-I) GILLIES M C; (PENF-I) PENFOLD P L  
CYC 95  
PI WO 2001049226 A1 20010712 (200148)\* EN 20 A61F009-00  
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TR TZ UG ZW  
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM  
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC  
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE  
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
AU 2001026527 A 20010716 (200169) A61F009-00  
EP 1253892 A1 20021106 (200281) EN A61F009-00  
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
RO SE SI TR  
US 2003060763 A1 20030327 (200325) A61M005-00  
JP 2003518987 W 20030617 (200349) 22 A61F009-007  
ADT WO 2001049226 A1 WO 2001-AU12 20010108; AU 2001026527 A AU 2001-26527  
20010108; EP 1253892 A1 EP 2001-901015 20010108, WO 2001-AU12 20010108; US  
2003060763 A1 WO 2001-AU12 20010108, US 2002-169230 20020912; JP  
2003518987 W JP 2001-549595 20010108, WO 2001-AU12 20010108  
FDT AU 2001026527 A Based on WO 2001049226; EP 1253892 A1 Based on WO

2001049226; JP 2003518987 W Based on WO 2001049226

PRAI AU 2000-4965 20000106

IC ICM A61F009-00; A61F009-007; A61M005-00

ICS A61M005-158

AB WO 200149226 A UPAB: 20010829

NOVELTY - A plaque (5) positioned over a patient's eye, comprises an inner surface which contacts the anterior surface of the eye, and an outer surface positioned which faces away from the eye. The inner surface has surface area equivalent to the exposed surface of the eye. The plaque is further provided with one or more guide units (6b), for guiding a needle into the interior of eye (pars plana).

DETAILED DESCRIPTION - The guide units are placed at a distance from the plaque which corresponds to center of iris. The plaque has a pair of opposed retaining units directed and dimensioned to ensure retraction of eye lids, when the plaque is placed over the eyes. The plaque has a control unit on the outer surface which regulates the penetration of needle into the eye. INDEPENDENT CLAIMS are also included for the following:

- (1) kit for use in intraocular injection of compound; and
- (2) guiding and administering an intraocular composition into the interior of a patient's eye.

USE - Useful for intravitreal administration of therapeutic agents, for treating intraocular conditions such as variety of exudative, edematous and inflammatory retinopathies such as **macular degeneration**, diabetic retinopathy, diabetic **macular** edema, cystoid **macular** edema, uveitis, endophthalmitis, retinal veno-occlusive disease, proliferative vitreo retinopathy, iritis, photodynamic therapy for **macular degeneration**, and also for application to aphakic eye.

ADVANTAGE - The plaque effectively immobilizes both the eye and eyelids during intraocular injection, prevents indentation of eye surface by penetration of needle and also allows correct angle of attack by needle, suitably at a distance from limbus and at suitable depth.

DESCRIPTION OF DRAWING(S) - The figure shows the illustration of the plaque in position over the eye with a needle being introduced through one of the guide unit.

Syringe 1

Needle 2

Plaque 5

Guide units 6b

Dwg.4/6

FS CPI GMPI

FA AB; GI; DCN

MC CPI: B11-C; B14-N03

TECH UPTX: 20010829

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compound: The compound which is introduced into the eye through needle is anti-inflammatory steroid, non-steroidal anti-inflammatory agent, metalloproteinase inhibitor, anti-angiogenic agent, antioxidant, anti-cytokine agent, anti-sense RNA, gene transfer vector, anti-viral, anti-fungal, antibiotic, anti-proliferative agent, anti-metabolite, tyrosine kinase inhibitor or calcium channel blocker. The compound is 11-substituted-16alpha,17alpha-substituted methylenedioxy steroid, preferably triamcinolone acetonide, flucinolone acetonide or **anecortave acetate**.

L75 ANSWER 5 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2001-432457 [46] WPIX

CR 2001-425112 [45]; 2002-672690 [72]; 2004-051015 [05]

DNN N2001-320495 DNC C2001-130762

TI New ophthalmic drug delivery device with geometry that facilitates it implantation on an outer surface of the sclera beneath the inferior oblique muscle, with the drug disposed above the macula.

DC A96 B05 B07 P32 P34



IN YAACOBI, Y  
PA (ALCO-N) ALCON UNIVERSAL LTD; (ALCO-N) ALCON INC; (YAAC-I) YAACOBI Y  
CYC 37  
PI WO 2001028474 A1 20010426 (200146)\* EN 41 A61F009-00  
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE  
W: AU BR CA CN JP KR MX PL TR US ZA  
AU 2001010812 A 20010430 (200148)  
US 6416777 B1 20020709 (200253) A61F002-14  
EP 1221919 A1 20020717 (200254) EN A61F009-00  
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
RO SE SI  
BR 2000014928 A 20021001 (200268) A61F009-00  
KR 2002060206 A 20020716 (200305) A61F009-00  
US 2003003129 A1 20030102 (200305) A61F002-00  
CN 1376042 A 20021023 (200313) A61F009-00  
JP 2003511205 W 20030325 (200330) 37 A61F009-007  
ZA 2002001189 A 20030430 (200334)# 49 A61F000-00  
AU 764226 B 20030814 (200363) A61F009-00  
MX 2002002925 A1 20020801 (200367) A61F009-00  
TW 539560 A 20030701 (200379) A61M035-00  
US 6669950 B2 20031230 (200402) A61F002-14  
AU 2003262099 A1 20031204 (200436) A61F009-00  
US 2004131654 A1 20040708 (200445) A61F002-00  
US 2004131655 A1 20040708 (200445) A61F002-00  
ADT WO 2001028474 A1 WO 2000-US28187 20001012; AU 2001010812 A AU 2001-10812  
20001012; US 6416777 B1 Provisional US 1999-160673P 19991021, US  
2000-664790 20000919; EP 1221919 A1 EP 2000-972099 20001012, WO  
2000-US28187 20001012; BR 2000014928 A BR 2000-14928 20001012, WO  
2000-US28187 20001012; KR 2002060206 A KR 2002-705022 20020419; US  
2003003129 A1 Provisional US 1999-160673P 19991021, Cont of US 2000-664790  
20000919, US 2002-187006 20020701; CN 1376042 A CN 2000-813192 20001012;  
JP 2003511205 W WO 2000-US28187 20001012, JP 2001-531071 20001012; ZA  
2002001189 A ZA 2002-1189 20020212; AU 764226 B AU 2001-10812 20001012; MX  
2002002925 A1 WO 2000-US28187 20001012, MX 2002-2925 20020315; TW 539560 A  
TW 2000-122134 20001020; US 6669950 B2 Provisional US 1999-160673P  
19991021, Cont of US 2000-664790 20000919, US 2002-187006 20020701; AU  
2003262099 A1 AU 2003-262099 20031112; US 2004131654 A1 Provisional US  
1999-160673P 19991021, Cont of US 2000-664790 20000919, Div ex US  
2002-187006 20020701, US 2003-697141 20031030; US 2004131655 A1  
Provisional US 1999-160673P 19991021, Cont of US 2000-664790 20000919, Div  
ex US 2002-187006 20020701, US 2003-697423 20031030  
FDT AU 2001010812 A Based on WO 2001028474; EP 1221919 A1 Based on WO  
2001028474; BR 2000014928 A Based on WO 2001028474; US 2003003129 A1 Cont  
of US 6416777; JP 2003511205 W Based on WO 2001028474; AU 764226 B  
Previous Publ. AU 2001010812, Based on WO 2001028474; MX 2002002925 A1  
Based on WO 2001028474; US 6669950 B2 Cont of US 6416777; AU 2003262099 A1  
Div ex AU 764226; US 2004131654 A1 Cont of US 6416777, Div ex US 6669950;  
US 2004131655 A1 Cont of US 6416777, Div ex US 6669950  
PRAI US 2000-664790 20000919; US 1999-160673P 19991021;  
US 2002-187006 20020701; ZA 2002-1189 20020212;  
US 2003-697141 20031030; US 2003-697423 20031030  
IC ICM A61F000-00; A61F002-00; A61F002-14; A61F009-00; A61F009-007;  
A61M035-00  
ICS A61K009-00; A61M037-00  
AB WO 200128474 A UPAB: 20040716  
NOVELTY - Device for delivering drugs to the human eye (which has a  
sclera, an inferior oblique muscle and a **macula**), comprising a  
pharmaceutically active agent and a geometry that facilitates an  
implantation of the device on an outer surface of the sclera beneath the  
inferior oblique muscle, the active agent being disposed above the  
**macula**, is new.  
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for  
delivering a pharmaceutically active agent to the human eye (which has a

sclera, an inferior oblique muscle and a **macula**), by providing:

(a) a drug delivery device comprising a pharmaceutically active agent; and

(b) disposing the device on an outer surface of the sclera, beneath the inferior oblique muscle, and with the active agent being disposed above the **macula**.

USE - The device is an implant for localized delivery of the pharmaceutically active agents to the posterior segment of the eye to combat age-related **macular degeneration (ARMD)**, choroidal neovascularization (CNV), retinopathies, retinitis, uveitis, **macular**, edema, glaucoma and neuropathies. Furthermore because of their capability to deliver a wide variety of actives, they are useful in clinical studies to deliver ophthalmic agents that create a specific physical condition in a patient.

ADVANTAGE - The invention provides improved devices and methods for safe, effective, rate-controlled, localized delivery of a variety of actives to the eye. The surgical procedure for implanting such devices is safe, simple, quick and capable of being performed in an outpatient setting. The devices are easy and economical to manufacture.

Dwg.0/21

FS CPI GMPI

FA AB; DCN

MC CPI: A12-V01; A12-V03D; B01-C06; B07-D05; B10-B02A; B11-C03; B11-C04A; B14-N03

TECH UPTX: 20010815

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Device: The geometry is generally F-, L- or C-shaped. The device further comprises: (a) a body with a scleral surface for placement proximate the outer surface of the sclera and a well with an opening to the scleral surface; and (b) an inner core disposed in the well comprising the active agent. The body comprises a biocompatible, non-bioerodable material. The body can comprise a polymeric composition, preferably consisting of one or more of the following polymers: silicone (preferred), polyvinyl alcohol, ethylene vinyl acetate, polylactic acid, nylon, polypropylene, polycarbonate, cellulose, cellulose acetate, polyglycolic acid, polylactic glycolic, cellulose esters, polyethersulfone and acrylics. The body is impermeable to the active. The inner core is tablet and can be semi-solid form in which is disposed the active. The body comprises an orbital surface with a radius of curvature that facilitates implantation of the device below Tenon's capsule. The scleral surface has a radius of curvature which is equal to the radius of curvature of the human eye. The active is nepafenac or is selected from 4,9(11)-pregnadien-17alpha,21-diol-3,20-dione and 4,9(11)-pregnadien-17alpha,21-diol-3,20-dione-21-acetate, eliprodil. The drug delivery device comprises a retaining member extending from the body proximate the opening. The body comprises a notch for facilitating the accommodation of the inferior oblique muscle during device implantation.

ABEX UPTX: 20010815

EXAMPLE - None given.

L75 ANSWER 6 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2001-425112 [45] WPIX

CR 2001-432457 [46]; 2002-672690 [72]; 2004-051015 [05]

DNN N2001-315406 DNC C2001-128562

TI Implantable drug delivery device for ophthalmic drug delivery, comprises body having an internal surface for placement proximate a target tissue and a well having an opening to the internal surface, and an inner core disposed in the well.

DC A96 B01 B07 P32

IN YAACOB, Y

PA (ALCO-N) ALCON UNIVERSAL LTD; (ALCO-N) ALCON INC

CYC 31

PI WO 2001028472 A1 20010426 (200145)\* EN 53 A61F009-00  
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AU BR CA CN JP KR MX PL TR US ZA  
 AU 2000073733 A 20010430 (200148)  
 EP 1221917 A1 20020717 (200254) EN A61F009-00  
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE  
 BR 2000014929 A 20021001 (200268) A61F009-00  
 KR 2002059630 A 20020713 (200306) A61F009-00  
 JP 2003515528 W 20030507 (200331) 32 A61K009-00  
 ZA 2002001188 A 20030430 (200334) 43 A61F000-00  
 MX 2002002338 A1 20020801 (200367) A61F009-00  
 AU 768400 B 20031211 (200404) A61F009-00  
 TW 555575 A 20031001 (200423) A61M037-00  
 ADT WO 2001028472 A1 WO 2000-US24983 20000912; AU 2000073733 A AU 2000-73733  
 20000912; EP 1221917 A1 EP 2000-961836 20000912; WO 2000-US24983 20000912;  
 BR 2000014929 A BR 2000-14929 20000912; WO 2000-US24983 20000912; KR  
 2002059630 A KR 2002-705020 20020419; JP 2003515528 W WO 2000-US24983  
 20000912; JP 2001-531069 20000912; ZA 2002001188 A ZA 2002-1188 20020212;  
 MX 2002002338 A1 WO 2000-US24983 20000912; MX 2002-2338 20020304; AU  
 768400 B AU 2000-73733 20000912; TW 555575 A TW 2000-120788 20001005  
 FDT AU 2000073733 A Based on WO 2001028472; EP 1221917 A1 Based on WO  
 2001028472; BR 2000014929 A Based on WO 2001028472; JP 2003515528 W Based  
 on WO 2001028472; MX 2002002338 A1 Based on WO 2001028472; AU 768400 B  
 Previous Publ. AU 2000073733, Based on WO 2001028472  
 PRAI US 1999-160673P 19991021  
 IC ICM A61F000-00; A61F009-00; A61K009-00; A61M037-00  
 ICS A61F009-007; A61K009-20; A61K031-575; A61K045-00; A61K047-30;  
 A61K047-32; A61K047-34; A61K047-38; A61P027-02  
 AB WO 200128472 A UPAB: 20040405

NOVELTY - A drug delivery device (I), comprising: (a) a body having an internal surface for placement proximate a target tissue and a well having an opening to the internal surface; and (b) an inner core disposed in the well comprising a pharmaceutically active agent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) delivering a pharmaceutically active agent to a target tissue within a body, comprising:

(a) providing a drug delivery device (I); and

(b) disposing the device within the body so that the pharmaceutically active agent is in communication with the target tissue through the opening;

(2) an ophthalmic drug delivery device, comprising:

(a) a body having a scleral surface for placement proximate a sclera and a well having an opening to the scleral surface; and

(b) an inner core disposed in the well comprising a pharmaceutically active agent;

(3) delivering a pharmaceutically active agent to an eye, the eye having a sclera, comprising the steps of:

(i) providing a drug delivery device comprising:

(a) a body having a scleral surface and a well having an opening to the scleral surface; and

(b) an inner core disposed in the well comprising a pharmaceutically active agent; and

(ii) disposing the device within the eye so that the pharmaceutically active agent is in communication with the sclera through the opening; and

(4) delivering a pharmaceutically active agent to the eye, the eye having a sclera, a Tenon's capsule, and a macula, comprising the steps of:

(a) providing a drug delivery device comprising a body having a pharmaceutically active agent disposed; and

(b) disposing the device on an outer surface of the sclera, below the Tenon's capsule, and proximate the macula.

USE - Implantable drug delivery device for ophthalmic drug delivery, especially for localized delivery of pharmaceutically active agents to the posterior segment of the eye to combat ARMD, CNV, retinopathies,

retinitis, uvetitis, macular edema and glaucoma.

ADVANTAGE - The device is safe, effective, rate controlled, and easy and economical to manufacture.

DESCRIPTION OF DRAWING(S) - Figure is a sectional view of drug delivery device.

drug delivery device 10

body 12

internal surface 14

external surface 16

proximal end 18

distal end 20

well 22

opening 24

inner core 26

retaining member 28

Dwg.1/7

FS CPI GMPI

FA AB; GI; DCN

MC CPI: A12-V02A; B01-C06; B04-C03; B07-D05; B11-C04A; B14-C03; B14-N03;  
B14-N04

TECH UPTX: 20010813

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The drug delivery device of body comprises a biocompatible, non-bioerodable material. The body comprises a polymeric composition.

Preferred Device: The drug delivery device further comprising a retaining member extending from the body proximate the opening. The inner core is a tablet, and comprises a hydrogel, the pharmaceutically active agent is disposed within the hydrogel. The body is impermeable to the pharmaceutically active agent. The internal surface has a geometry that mates with a surface of the target tissue. The device is surgically implantable into a body. The pharmaceutically active agent comprises a compound selected from 4,9(11)-Pregnadien-17alpha,21-diol-3,20-dione and 4,9(11)-Pregnadien-17alpha,21-diol-3,20-dione-21-acetate. The pharmaceutically active agent comprises eliprodil.

Preferred Method: The method comprising the step of delivering a pharmaceutically effective amount of the pharmaceutically active agent to the target tissue for a period of time. The scleral surface has a geometry that mates with the sclera. The device is surgically implantable into an eye, and further comprising an orbital surface having at least one tapered surface that facilitates implantation of the device. The eye is a human eye having a macula, and the disposing step comprises disposing the device generally above the macula. The human eye having a choroid and a retina, and further comprising the step of delivering a pharmaceutically effective amount of the pharmaceutically active agent through the sclera and the choroid and to the retina over a period of time.

TECHNOLOGY FOCUS - POLYMERS - Preferred Composition: The polymeric composition comprises one or more polymers selected from silicone, polyvinyl alcohol, ethylene vinyl acetate, polylactic acid, nylon, polypropylene, polycarbonate, cellulose, cellulose acetate, polyglycolic acid, polylactic glycolic acid, cellulose esters, polyethersulfone, and acrylics.

=> d 3 5 6 dcN

L76 ANSWER 3 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

M5 \*04\* DCN: RA0EF8-K; RA0EF8-T; RA0EF8-M

M5 \*05\* DCN: R00141-K; R00141-T; R00141-M

M5 \*06\* DCN: R06358-K; R06358-T; R06358-M; R06359-K; R06359-T; R06359-M

M5 \*07\* DCN: 0071-89406-K; 0071-89406-T; 0071-89406-M

M5 \*08\* DCN: 0071-89403-K; 0071-89403-T; 0071-89403-M

M5 \*09\* DCN: 0071-89401-K; 0071-89401-T; 0071-89401-M

M5 \*10\* DCN: 0071-89409-K; 0071-89409-T; 0071-89409-M  
M5 \*11\* DCN: 0071-89408-K; 0071-89408-T; 0071-89408-M  
M5 \*12\* DCN: 0071-89404-K; 0071-89404-T; 0071-89404-M  
M5 \*13\* DCN: 0071-89407-K; 0071-89407-T; 0071-89407-M  
M5 \*14\* DCN: 0071-89405-K; 0071-89405-T; 0071-89405-M  
M5 \*15\* DCN: 0071-89402-K; 0071-89402-T; 0071-89402-M

## L76 ANSWER 5 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

M2 \*01\* DCN: RA0590-K; RA0590-T; RA0590-M  
M2 \*02\* DCN: R04971-K; R04971-T; R04971-M  
M2 \*03\* DCN: RA01ZO-K; RA01ZO-T; RA01ZO-M  
M2 \*04\* DCN: 0033-63609-K; 0033-63609-T; 0033-63609-M  
M2 \*05\* DCN: 0033-63608-K; 0033-63608-T; 0033-63608-M  
M2 \*06\* DCN: 0033-63607-K; 0033-63607-T; 0033-63607-M  
M5 \*07\* DCN: **RA0EF8-K; RA0EF8-T; RA0EF8-M**  
M5 \*08\* DCN: 0033-63606-K; 0033-63606-T; 0033-63606-M  
M5 \*09\* DCN: 0033-63605-K; 0033-63605-T; 0033-63605-M  
M5 \*10\* DCN: 0033-63604-K; 0033-63604-T; 0033-63604-M  
M5 \*11\* DCN: 0033-63603-K; 0033-63603-T; 0033-63603-M  
M5 \*12\* DCN: 0033-63602-K; 0033-63602-T; 0033-63602-M  
M5 \*13\* DCN: 0033-63601-K; 0033-63601-T; 0033-63601-M

## L76 ANSWER 6 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

M2 \*14\* DCN: 0004-46908-K; 0004-46908-U  
M5 \*01\* DCN: RA0EF4-K; RA0EF4-U  
M5 \*02\* DCN: RA0EF5-K; RA0EF5-U  
M5 \*03\* DCN: RA0EF6-K; RA0EF6-U  
M5 \*04\* DCN: RA0EF7-K; RA0EF7-U  
M5 \*05\* DCN: **RA0EF8-K; RA0EF8-U**  
M5 \*06\* DCN: RA0EF9-K; RA0EF9-U  
M5 \*07\* DCN: 0004-46901-K; 0004-46901-U  
M5 \*08\* DCN: 0004-46902-K; 0004-46902-U  
M5 \*09\* DCN: 0004-46903-K; 0004-46903-U  
M5 \*10\* DCN: 0004-46904-K; 0004-46904-U  
M5 \*11\* DCN: 0004-46905-K; 0004-46905-U  
M5 \*12\* DCN: 0004-46906-K; 0004-46906-U  
M5 \*13\* DCN: 0004-46907-K; 0004-46907-U

=> d 170 all

## L70 ANSWER 1 OF 1 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

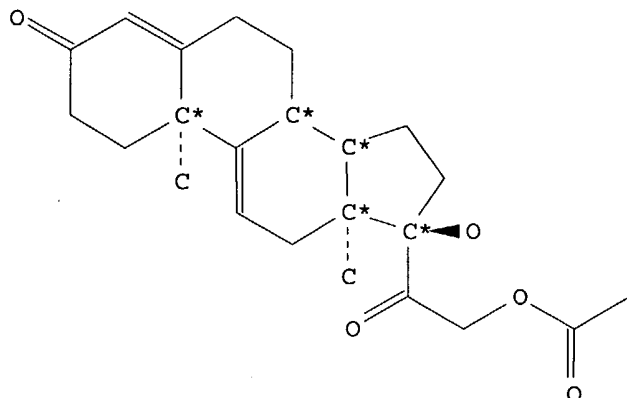
AN.S DCR-219509

DCSE 219509-1-0-0

CN.P ANECORTAVE

CN.S 4,9(11)-Pregnadien-17alpha,21-Diol-3,20-Dione-21-Acetate; Acetic acid  
2-(17-hydroxy-10,13-dimethyl-3-oxo-2,3,6,7,8,10,12,13,14,15,16,17-  
dodecahydro-1H-cyclopenta[a]phenanthren-17-yl)-2-oxo-ethyl ester

SY AL-3789; **ANECORTAVE**



MF C23 H30 O5  
 SMF C23 H30 O5 \*1; TOTAL \*1; TYPE \*1  
 MW 386.4926  
 SDCN RA0EF8  
 CC STEROIDS  
 SMIL CC(=O)OCC(=O)C1(O)CCC2C3CCC4=CC(=O)CCC4(C)C3=CCC21C  
 ISMI CC(=O)OCC(=O)[C@@]1(O)CC[C@H]2[C@@H]3CCC4=CC(=O)CC[C@]4(C)C3=CC[C@@]21C

=> d 176 all abeq tech abex tot

L76 ANSWER 1 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN  
 AN 2003-863951 [80] WPIX  
 DNC C2003-244196  
 TI Treatment and/or prevention of central nervous system disorders and/or states involves administration of a pharmaceutical composition by an ocular route of drug delivery.  
 DC A96 B05 B07 D22  
 IN ABDULRAZIK, M  
 PA (ABDU-I) ABDULRAZIK M  
 CYC 1  
 PI US 2003181354 A1 20030925 (200380)\* 17 A61K031-00  
 ADT US 2003181354 A1 US 2003-354173 20030130  
 PRAI IL 2002-147921 20020131  
 IC ICM A61K031-00  
 AB US2003181354 A UPAB: 20031211  
 NOVELTY - Treatment and/or prevention of central nervous system disorders and/or states involves administration of a pharmaceutical composition (A) by an ocular route of drug delivery.  
 DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for method (M) for the treatment of migraines in humans involving:  
 (a) administering a pharmaceutical composition (A') by an ocular route of drug delivery; or  
 (b) administering an established anti-migraine therapeutic agent by an ocular route of drug delivery.  
 ACTIVITY - CNS-Gen.; Vasotropic; Tranquilizer; Analgesic; Antimigraine; Neuroprotective; Anticonvulsant; Antiparkinsonian; Nootropic; Muscular-Gen.; Cytostatic; Antibacterial; Antiinflammatory; Antidepressant; Neuroleptic; Antiaddictive; Eating-disorder-Gen.; Anorectic; Hypotensive; Auditory; Ophthalmological; Antiangiogenic; Cerebroprotective; Immunosuppressive; Antiarthritic; Antiarteriosclerotic; Anabolic; Immunomodulator; Uropathic; Sedative; Endocrine-Gen.; Hypnotic; Antimicrobial; Antialcoholic; Antismoking.  
 A 48-year old female patient with a history of migraine, and right eye primary open angle glaucoma was prescribed with brimonidine tartrate

(0.2%) as a second topical antiglaucoma agent. The patient reported a substantial relief of migraine related symptoms.

MECHANISM OF ACTION - None given.

USE - For the treatment and/or prevention of central nervous system disorders and/or states in human or animal e.g. central nervous system ischemia, central nervous system reperfusion injury, spinal ischemia, central nervous system trauma, crushed or compressed optic nerve, headache, migraine, pain, multiple sclerosis, optic neuritis, optic neuropathies, ocular glaucomatous damage, epilepsy, convulsions, neurodegenerative diseases, Parkinson's disease, Alzheimer's disease, ataxias, dystonias, movement disorders, choreas, intracranial tumors, intracranial metastasis, intracranial infections, meningitis, central nervous system states in need of cognition enhancement, memory disorders, depression, avoidant personality disorder, anxiety, panic disorder, obsessive-compulsive disorders, phobias, impulsive disorders, cognitive disorders, mood disorders, psychoses, schizophrenia, drug abuse, chemical dependencies, drugs tolerance or withdrawal, posttraumatic stress syndrome, eating disorders, obesity premature ejaculation, hypertension, aminoglycoside antibiotics-induced hearing loss, central nervous system drug-induced disorders and states, N-methyl-D-aspartate-induced neurodegeneration, glutamate induced excitotoxic effects on nerve cells, central nervous system metabolic disorders and states, central nervous system deficiency disorders, central nervous system disorders and states amenable to neuropeptides therapy, central nervous system disorders and states amenable to neurotrophic factors therapy, central nervous system disorders and states amenable to neuroprotective therapy, central nervous system mediated ocular glaucomatous damage, autoimmune glaucoma, central nervous system disorders and states amenable to gene-therapy, surgically-induced inflammation, trauma-induced inflammation, angiogenesis-related disorder, hypoproliferative diseases, brain or spinal cord disease, disorder or injury, conditions which can lead to excessive glutamate release, conditions which can lead to neurodegeneration, stroke, impaired blood flow in neuronal tissue, septic or traumatic shock, hemorrhage shock, arthritis, arteriosclerosis, conditions which can lead to bursting of the myelin sheath around nerves, senile dementia, Huntington's disease, Lou Gehrig's disease (ALS), addictive disorders to at least one of alcohol, nicotine, and other psychoactive substance, adjustment disorder, age-associated learning and mental disorder, anorexia nervosa, apathy, attention-deficit disorder due to general medical conditions, attention-deficit hyperactivity disorder, bipolar disorder, bulimia nervosa, chronic fatigue syndrome, chronic or acute stress, conduct disorder, cyclothymic disorder, dizziness, dysthymic disorder, fibromyalgia and other somatoform disorders, incontinence, inhalation disorder, insomnia, intoxication disorder, obesity, peripheral neuropathy, premenstrual dysphoric disorder, psychotic disorder, seasonal affective disorder, sexual dysfunction, sleep disorder (e.g. narcolepsy and enuresis), specific developmental disorder, TIC disorders (e.g. Tourette's disease and withdrawal syndrome) (claimed).

ADVANTAGE - The method achieves effective CNS target site concentrations of the drugs, while limiting systemic exposure and distribution of the drug to peripheral sites of action. Thus lessens unwanted side effects and the potential for toxicity.

Dwg.0/8

FS CPI

FA AB; DCN

MC CPI: A12-V01; B01-C03; B06-D06; B06-E03; B06-F03; B07-D09; B07-E01; B07-F02; B09-D01; B10-A17; B10-D03; B10-E04; B14-C01; B14-C03; B14-C09; B14-D01; B14-E11; B14-F02C; B14-F02D; B14-F02D1; B14-F05; B14-H01B; B14-J01; B14-J01A3; B14-J01B3; B14-J05; B14-J05C; B14-J07; B14-L01; B14-M01A; B14-M01B; B14-M01C; B14-N03; B14-N07D; B14-N09; B14-N16; B14-P02; B14-S01; B14-S06; B14-S07; D09-A; D09-C01

TECH UPTX: 20031211

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: (A) comprises

N-methyl-D-aspartate receptor antagonist (preferably memantine); alpha-2 adrenoreceptor agonist (preferably alpha-2 adrenoreceptor subtype specific agonist) (preferably brimonidine); beta-blocker; established anti-cancer therapeutics, their derivatives, prodrugs and/or codrugs; established anti-Parkinsonian therapeutics or their combinations; recombinant adeno-associated virus, other established gene-therapy vectors and/or other gene delivery systems; zinc derivatives, magnesium derivatives, vitamins and/or multi-vitamins; established ophthalmic therapeutics, their derivatives, prodrugs and/or codrugs; prostaglandin analogues, their derivatives, prodrugs and/or codrugs; prostamid receptor agonist (preferably bimatoprost); cannabinoid receptors agonists; steroid (preferably angiostatic steroid, especially **anecortave**); imino-imidazoline (preferably clonidine or apraclonidine); catecholamine; alpha-2 adrenergic agonist (preferably quinoxaline). The alpha-2 adrenoreceptor agonist is selected from imidazoline (preferably naphazoline, xymetazoline, tetrahydrozoline or tramazoline), imidazole (preferably detomidine, medetomidine or dexmedetomidine), azepine (preferably B-HT 920 (6-allyl-2-amino-5,6,7,8-tetrahydro-4H-thiazolo(4,5-d)-azepine) or B-HT 933), thiazines (preferably xylazine), thiazine (preferably xylazine), oxazoline (preferably rilmenidine), or guanidine (preferably guanabenz or guanfacine). Quinoxaline is selected from (2-imidazolin-2-ylamino) quinoxaline, 5-halide-6-(2-imidazolin-2-ylamino) quinoxaline or tartrate of 5-bromo-6-(2-imidazolin-2-ylamino) quinoxaline. The prostaglandin analogue is selected from latanoprost, unoprostone, travaprost or bimatoprost. (A') comprises alpha-2 adrenoreceptor antagonist and also includes brimonidine tartrate. Preferred Method: Method (A) further involves administering an established anti-migraine therapeutic agent in combination with (A'). The established anti-migraine therapeutic agent is administered systemically or ocularly. Brimonidine tartrate is administered ocularly in a composition containing (0.0001 - 9)% brimonidine tartrate.

ABEX

UPTX: 20031211

ADMINISTRATION - The ocular route of drug delivery involves delivery by eye-drop, suspension, ointment, gel, hydrogel and viscosified solution system, gel-forming system, lotion, spray, liposome, emulsion, strip, therapeutic contact lenses, membrane-bound devices, collagen shield, insert, polymeric dosing system, rod-like insert, iontophoresis, anterior chamber dosing, sub-conjunctival dosing or implant, subtenon dosing or implant, retrobulbar dosing or implant, peribulbar dosing or implant, trans-septal dosing or implant, choroidal dosing or implant, ciliary body dosing or implant, subretinal dosing or implant, intra-vitreous dosing or implant, intraocular implantable or injected sustained release system, encapsulated cell technology dosing system, transscleral drug delivery system, optic nerve related dosing system, infusion to ocular tissue via a pump-catheter system, drug incorporation in surgical irrigating solution or ocular dosing of gene-therapy vector (claimed).

EXAMPLE - No relevant example given.

L76 ANSWER 2 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN  
 AN 2003-221819 [21] WPIX  
 DNN N2003-176875 DNC C2003-056583  
 TI Ocular iontophoretic device for non-invasive delivery of a steroid composition to the eye, is useful for treating inflammatory or neovascularization conditions.  
 DC B01 B07 D22 P34 S05  
 IN LLOYD, L B; PARKINSON, T M; SZLEK, M  
 PA (LLOY-I) LLOYD L B; (PARK-I) PARKINSON T M; (SZLE-I) SZLEK M; (IOME-N) IOMED INC  
 CYC 100  
 PI WO 2003008036 A2 20030130 (200321)\* EN 26 A61N000-00  
 RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW



W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

US 2003023228 A1 20030130 (200325) A61M031-00

AU 2002316723 A1 20030303 (200452) A61N000-00

ADT WO 2003008036 A2 WO 2002-US22859 20020719; US 2003023228 A1 US 2001-910443  
20010720; AU 2002316723 A1 AU 2002-316723 20020719

FDT AU 2002316723 A1 Based on WO 2003008036

PRAI US 2001-910443 20010720

IC ICM A61M031-00; A61N000-00

AB WO2003008036 A UPAB: 20030328

NOVELTY - An ocular iontophoretic device for non-invasive delivery of a steroid composition to the eye, comprises an active electrode assembly associated with a matrix, where the matrix includes a corticosteroid, **anecortave** phosphate steroid or amino sterole composition, particularly dexamethasone, for treating inflammatory and/or neovascularization conditions.

ACTIVITY - Ophthalmological; Antiinflammatory.

MECHANISM OF ACTION - None given.

USE - The device is for the delivery of steroid compositions to the eye, especially in the treatment of inflammatory or neovascularization conditions.

ADVANTAGE - Compared to previous delivery methods, the device enables a generally painless, non-invasive and deep delivery of a steroid composition. The composition is locally delivered to an affected area of the eye at an effective, therapeutic level.

Dwg.0/3

FS CPI EPI GMPI

FA AB; DCN

MC CPI: B01-B02; B11-C04; B12-M10A; B14-C03; B14-F02F; B14-N03; D09-C04

EPI: S05-A07

TECH UPTX: 20030328

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The dexamethasone composition has molecular weight 400-600. Preferred compositions include dexamethasone sodium phosphate, and esters, e.g. 9-fluoro 11beta,17-dihydroxy-16alpha-methyl-21-(phosphonoxy)pregna-1,4-diene 3,20-dione disodium salt. The composition comprises 0.5-4, preferably 1 wt.% of compound. The buffer pH is 6-8.5, preferably 7.4. Preferred Device: The device may further comprise a counter electrode assembly, completing an electrical circuit between the active electrode assembly and an energy source, and an energy source for generating electrical potential difference. The active electrode assembly includes an open-faced or high current density electrode. The device is positioned on the conjunctival surface in a region of a pars planum and/or insertions of an anterior ciliary artery.

ABEX UPTX: 20030328

ADMINISTRATION - Administration is into the vitreous humor, retina, choroids, circulation of the retina, circulation of the choroid, or sclera. The composition is iontophoretically delivered at 0.5-4 mA for 5-20 minutes.

L76 ANSWER 3 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2002-643247 [69] WPIX

DNC C2004-014126

TI Composition useful for controlling and lowering intraocular pressure comprises an angiostatic agent and at least one intraocular pressure lowering compound.

DC B01

IN CLARK, A F

PA (ALCO-N) ALCON LAB INC; (ALCO-N) ALCON MFG LTD

CYC 30

PI WO 2002040030 A1 20020523 (200269)\* EN 19 A61K031-56

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR  
W: AU BR CA CN JP KR MX PL US ZA  
AU 2001017709 A 20020527 (200269) A61K031-56  
EP 1341541 A1 20030910 (200367) EN A61K031-56  
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR  
JP 2004522711 W 20040729 (200452) 36 A61K045-06  
ADT WO 2002040030 A1 WO 2000-US31557 20001116; AU 2001017709 A WO 2000-US31557  
20001116, AU 2001-17709 20001116; EP 1341541 A1 EP 2000-980450 20001116,  
WO 2000-US31557 20001116; JP 2004522711 W WO 2000-US31557 20001116, JP  
2002-542403 20001116  
FDT AU 2001017709 A Based on WO 2002040030; EP 1341541 A1 Based on WO  
2002040030; JP 2004522711 W Based on WO 2002040030  
PRAI WO 2000-US31557 20001116  
IC ICM A61K031-56; A61K045-06  
ICS A61K031-138; A61K031-5377; A61K031-5575; A61K031-57; A61P009-00;  
A61P027-02  
AB WO 2002040030 A UPAB: 20040429  
NOVELTY - A composition comprises an angiostatic agent (I) or (II) and at  
least one other compound (III) which lowers intraocular pressure (IOP).  
ACTIVITY - Ophthalmological; Hypotensive.  
MECHANISM OF ACTION - Glycosaminoglycan Inhibitor.  
No biological data given.  
USE - For lowering and controlling intraocular pressure (IOP)  
(claimed), and in the treatment of glaucoma and ocular hypertension.  
ADVANTAGE - The composition provides effective, long duration control  
of intraocular pressure (IOP) with less IOP spiking.  
Dwg.0/0  
FS CPI  
FA AB; GI; DCN  
MC CPI: B01-A02; B01-B03; B01-B04; B01-C07; B07-D09; B07-E03; B07-F01;  
B10-B03B; B14-F02B; B14-N03  
TECH UPTX: 20040429  
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The angiostatic  
agent is a compound of formula (I), (II) or their salts.  
R1 = H, -CH3 or -C2H5;  
R2 = F, 9-11C double bond, 9-11C epoxy, H or Cl;  
R3 = H, OR26, OC(=O)R27, halo, 9-11C double bond, 9-11C epoxy, =O, -OH,  
-O-1-12C alkyl, -OC(=O)-1-12C alkyl, -OC(=O)-Ar, -OC(=O)N(R)2 or  
-OC(=O)OR7;  
Ar = furyl, thienyl, pyrrolyl or pyridyl (all optionally substituted with  
1-2 1-4C alkyl) or (CH2)f-phenyl (phenyl is optionally substituted with  
1-3 T);  
T = Cl, F, Br, 1-3C alkyl, 1-3C alkoxy, 1-3C thioalkoxy, Cl3C-, F3C-, -NH2  
or -NHC(=O)CH3;  
R = H, 1-4C alkyl or phenyl;  
R7 = Ar or 1-12C alkyl;  
R4 = H, CH3, Cl or F;  
R5 = R4, OH, Br, phenyl, vinyl or allyl;  
R6 = H or CH3;  
R9 = CH2CH2OR26, CH2CH2OC(=O)R27, H, OH, CH3, F, =CH2, CH2C(=O)OR28, OR26,  
O(C=O)R27 or O(C=O)CH2(C=O)OR26;  
R10 = -CCH, -CH=CH2, halo, CN, N3, OR26, OC(=O)R27, H, OH, CH3 or a double  
bond between C-16 and C-17;  
R12, R14 = H; or  
R12+R1, R12+R14 = double bond;  
R13 = halo, OR26, OC(=O)R27, NH2, NHR26, NHC(=O)R27, N(R26)2, NC(=O)R27,  
N3, H, -OH, =O, -O-P(=O)(OH)2 or -O-C(=O)-(CH2)t-COOH;  
t = 2-6;  
R15 = H, =O or -OH;  
R10+R23 = cyclic phosphate;  
R23 = -OH, O-C(=O)-R11, -OP(O)-(OH)2 or -O-C(=O)-(CH2)tCOOH;  
R11 = -Y-(CH2)n-X-(CH2)m-SO3H, -Y'-(CH2)p-X'-(CH2)q-NR16R17 or -Z(CH2)r-Q;  
Y, Z = bond or -O-;

Y' = bond, -O- or -S-;  
 X, X' = bond, -CON(R18)-, -N(R18)CO-, -O-, -S-, -S(O)- or -S(O2)-;  
 R18 = H or 1-4C alkyl;  
 R16, R17 = 1-4C lower alkyl optionally substituted by OH; or  
 NR16R17 = monocyclic heterocycle selected from pyrrolidino, piperidino, (thio)morpholino, piperazino or N(1-4C lower alkyl)-piperazino;  
 n = 4-9;  
 m, q = 1-5;  
 p, r = 2-9;  
 Q = -R19-CH2COOH, -CO-COOH or CON(R21)CH(R22)COOH;  
 R19 = -S-, -S(O)-, -S(O)2, -S(O)2N(R20)- or N(R20)SO2-;  
 R20 = H or 1-4C lower alkyl;  
 R21 = H or CH3;  
 R22 = H, CH3, -CH2COOH, -CH2CH2COOH, -CH2OH, -CH2SH, -CH2CH2SCH3 or -CH2Ph-OH (where Ph-OH is para hydroxyphenyl); or  
 R21+R22 = -CH2CH2CH2-; or  
 -N(R21)CH(R22)COOH = -NHCH2CONHCH2COOH;  
 R24 = CH, C1-C2 double bond, or O;  
 R25 = C(R15)CH2-R23, OH, OR26, OC(=O)R27, R26, COOH, C(=O)OR26, CHOHCH2OH, CHOHCH2OR26, CHOHCH2OC(=O)R27, CH2CH2OH, CH2CH2OR26, CH2CH2OC(=O)R27, CH2CN, CH2N3, CH2NH2, CH2NHR26, CH2N(R26)2, CH2OH, CH2OR26, CH2O(C=O)R27, CH2O(P=O)(OH)2, CH2O(P=O)(OR26)2, CH2SH, CH2S-R26, CH2SC(=O)R27, CH2NC(=O)R27, C(=O)CHR28OH, C(=O)CHR28OR26, or C(=O)CHR28OC(=O)R27; or  
 R10+R25 = C(R28)2 that is an optionally alkyl substituted methylene group;  
 R26 = 1-6C (optionally branched alkyl, cycloalkyl, haloalkyl, aralkyl or aryl);  
 R27 = R26+OR26; and  
 R28 = H or 1-6C (optionally branched alkyl or cycloalkyl);  
 provided that the total number of carbon atoms in R20 and (CH2)r is at least 10; when R21 is CH3, R22 is H. (III) is selected from miotics, sympathomimetics, beta-blocker (preferably timolol, betaxolol or levobetaxolol), carbonic anhydrase inhibitors or prostaglandins.

ABEX

UPTX: 20040429

SPECIFIC COMPOUNDS - Use of 4,9(11) Pregnadien-17,21-diol-21-acetate (Ia) as the angiostatic agent is specifically claimed.

ADMINISTRATION - The composition is administered topically to the affected eye, 1-2 drops, 1-4 times per day.

EXAMPLE - A composition comprised of (weight%): timolol maleate (0.68), 4,9(11) pregnadien-17,21-diol-3; 20-dione-21-acetate (1), mannitol (2.4), sodium chloride (0.4), Carbopol 974P (RTM; drug carrier substance) (0.5), polysorbate 80 (0.05), edetate disodium (0.01), benzalkonium chloride (0.01), NaOH (to pH 7.4) and purified water (balance to 100 ml).

L76 ANSWER 4 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2002-627225 [67] WPIX

DNN N2004-028639 DNC C2004-012568

TI Reduction or prevention of transplant rejection in an eye involves use of bioerodible drug delivery system comprising an immunosuppressive agent and a bioerodible polymer.

DC A96 B05 B07 D22 P32 P34

IN WONG, V G

PA (OCUL-N) OCULEX PHARM INC; (ALLR) ALLERGAN INC; (WONG-I) WONG V G

CYC 100

PI WO 2002043785 A2 20020606 (200267)\* EN 33 A61L027-00

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
 NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
 RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002036495 A 20020611 (200267) A61L027-00

US 2002182185 A1 20021205 (200301) A61K045-00  
 EP 1339438 A2 20030903 (200365) EN A61L027-54  
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI TR

BR 2001015772 A 20040113 (200409) A61L027-00  
 US 6699493 B2 20040302 (200417) A61F002-14  
 JP 2004514702 W 20040520 (200434) 64 A61K045-00  
 US 2004137034 A1 20040715 (200447) A61F002-00  
 JP 2004210798 A 20040729 (200450) 23 A61K031-573

ADT WO 2002043785 A2 WO 2001-US44481 20011128; AU 2002036495 A AU 2002-36495  
 20011128; US 2002182185 A1 Provisional US 2000-250023P 20001129,  
 Provisional US 2001-298253P 20010612, US 2001-997094 20011128; EP 1339438  
 A2 EP 2001-986027 20011128, WO 2001-US44481 20011128; BR 2001015772 A BR  
 2001-15772 20011128, WO 2001-US44481 20011128; US 6699493 B2 Provisional  
 US 2000-250023P 20001129, Provisional US 2001-298253P 20010612, US  
 2001-997094 20011128; JP 2004514702 W WO 2001-US44481 20011128, JP  
 2002-545755 20011128; US 2004137034 A1 Provisional US 2000-250023P  
 20001129, Provisional US 2001-298253P 20010612, Cont of US 2001-997094  
 20011128, US 2003-744560 20031222; JP 2004210798 A Div ex JP 2002-545755  
 20011128, JP 2004-121618 20040416

FDT AU 2002036495 A Based on WO 2002043785; EP 1339438 A2 Based on WO  
 2002043785; BR 2001015772 A Based on WO 2002043785; JP 2004514702 W Based  
 on WO 2002043785; US 2004137034 A1 Cont of US 6699493

PRAI US 2001-298253P 20010612; US 2000-250023P 20001129;  
 US 2001-997094 20011128; US 2003-744560 20031222

IC ICM A61F002-00; A61F002-14; A61K031-573; A61K045-00; A61L027-00;  
 A61L027-54  
 ICS A01N025-10; A61K009-00; A61K031-4745; A61K031-522; A61K031-525;  
 A61K031-57; A61K038-00; A61K038-13; A61K047-30; A61K047-32;  
 A61K047-34; A61K047-38; A61P027-02; A61P037-06; A61P041-00;  
 A61P043-00

AB WO 200243785 A UPAB: 20040608  
 NOVELTY - Reduction or prevention of transplant rejection in an eye of an  
 individual involves:  
 (a) performing an ocular transplant procedure on the eye and  
 (b) placing in the eye a bioerodible drug delivery system (I)  
 comprising an immunosuppressive agent (Ia) and a bioerodible polymer (Ib).  
 DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a kit  
 comprising (I) and instructions for use. (I) is designed to be implanted  
 in the eye.  
 ACTIVITY - Immunosuppressive; ophthalmological;  
 MECHANISM OF ACTION - None given.  
 USE - In the manufacture of bioerodible drug delivery system for  
 reducing or preventing transplant rejection in an eye of an individual/  
 e.g. human (claimed).  
 ADVANTAGE - The drug delivery system is made of a biodegradable  
 polymer matrix which can release drug loads over various programmed time  
 periods.  
 Dwg.0/0

FS CPI GMPI  
 FA AB; DCN  
 MC CPI: A05-E02; A12-V01; A12-V02A; B01-B02; B01-C04; B02-C; B04-C02A2;  
 B04-C03C; B06-D02; B06-D06; B06-D09; B06-E05; B07-A02A; B07-D04B;  
 B07-D09; B07-D12; B07-D13; B10-A17; B12-M10; B14-G02; B14-G02C;  
 B14-N03; D09-C01

TECH UPTX: 20040426  
 TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The method involves  
 implanting into the eye a solid body comprising particles of (Ia)  
 entrapped within (Ib). (Ia) is released from the solid body by erosion of  
 (Ib). The ocular transplant procedure is a retinal pigment epithelium  
 (RPE) transplant or a cornea transplant. (I) is placed in the anterior  
 chamber or vitreous cavity of the eye.  
 Preferred Delivery System: (I) comprises (wt.%):

- (i) dexamethasone or cyclosporin A (50, preferably 60) and PLGA (40, preferably 50) or
- (ii) dexamethasone or cyclosporin A (50), hydroxy propyl methyl cellulose (HPMC) (15) and PLGA (35).

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: (Ib) is a polymer or polylactic acid polyglycolic acid (PLGA) copolymer. The implant further comprises (HPMC) (15 wt.%).

ABEX UPTX: 20040426

SPECIFIC COMPOUNDS - Dexamethasone, cyclosporin A, azathioprine, brequinar, gusperimus, 6-mercaptopurine, mizoribine, rapamycin, (FK-506) (tacrolimus), denopterin, edatrexate, methotrexate, piritrexim, pteropterin, Tomudex, trimetrexate, cladribine, fludarabine, 6-mercaptopurine, thiamiprine, thiaguanine, ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, doxifluridine, emitefur, enocitabine, floxuridine, fluorouracil, gemcitabine, egafur, fluocinolone, triaminolone, **anecortave acetate**, fluorometholone, medrysone and prednisolone are specifically claimed as (Ia).

ADMINISTRATION - (I) is administered via intraocular implants for at least about 5 days.

EXAMPLE - Dexamethasone powder (2100 mg) was mixed with 50/50 polylactic acid polyglycolic acid (PLGA) (900 mg) at ambient temperature. A small Teflon tube was filled with the mixture (900 - 1100 mug) and placed directly on the die cavity. The powder was pressed using a tablet press, ejected and removed to obtain a pellet (approximately 2 mm x 0.75 mm). Release of dexamethasone from DEXPS DDS system was measured. The concentration values were used to calculate the cumulative release and showed that % total release of dexamethasone on day 1 and day 35 was 10.1 and 88.1 respectively.

L76 ANSWER 5 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2001-167739 [17] WPIX

DNC C2001-049955

TI Composition useful in treatment of glaucoma and ocular hypertension comprises angiostatic steroid compound in combination with intraocular pressure lowering agent.

DC B01

IN CLARK, A F

PA (ALCO-N) ALCON LAB INC

CYC 1

PI US 6172054 B1 20010109 (200117)\* 7 A61K031-56

ADT US 6172054 B1 US 1995-491005 19950615

PRAI US 1995-491005 19950615

IC ICM A61K031-56

AB US 6172054 B UPAB: 20010328

NOVELTY - Composition comprises an angiostatic steroid compound (I) or (II) in combination with an intraocular pressure lowering agent (III).

DETAILED DESCRIPTION - Composition comprises an angiostatic steroid compound of formula (I) or (II) or their salts and at least one intraocular pressure (IOP) lowering compound (III) comprising miotics, sympathomimetics, beta-blockers, carbonic anhydrase inhibitors and/or prostaglandins.

R1 = H, beta-methyl or beta-ethyl;

R2 = F, 9-11C double bond, 9-11C 1-epoxy, H or Cl;

R3 = H, OR26, OC(=O)R27, halo, 9-11C double bond, 9C-Cl, 1-epoxy, =O, OH, 1-12C alkoxy, -OC(=O)1-12C alkyl, -OC(=O)aryl, -OC(=O)N(R)2 or -OC(=O)OR7;

aryl = furyl, thienyl, pyrrolyl or pyridyl (all optionally substituted by one or two 1-4C alkyl) or -(CH2)f-phenyl in which f is 0-2 and the phenyl ring is optionally substituted by 1-3 Cl, Br, F, 1-3C alkyl, 1-3C alkoxy, 1-3C thioalkoxy, CCl3, CF3, NH2 or NHCOCH3;

R = H, 1-4C alkyl or phenyl;  
 R4 = H, CH3, Cl or F;  
 R5 = H, OH, F, Cl, Br, CH3, phenyl, vinyl or allyl;  
 R6 = H or CH3;  
 R9 = CH2CH2OR26, CH2CH2OC(=O)R27, H, OH, CH3, F, =CH2, CH2C(=O)OR28,  
 OR26, O(C=O)R27 or O(C=O)CH2(C=O)OR26;  
 R10 = -C triple bond CH, -CH=CH2, halo, CN, N3, OR26, OC(=O)R27, H,  
 OH, CH3 or R10 forms a second bond between positions C-16 and C-17;  
 R12 = H or forms a double bond with R1 or R14;  
 R13 = halo, OR26, OC(=O)R27, NH2, NHR26, NHC(=O)R27, N(R26)2,  
 NC(=O)R27, N3, H, OH, =O, -O-P(=O)(OH)2 or O-C(=O)-(CH2)tCOOH;  
 R14 = H or forms double bond with R12;  
 R15 = H, =O or OH;  
 R23 = OH, O-C(=O)-R11, -OP(O)-(OH)2 or -O-C(=O)-(CH2)tCOOH, or  
 R23 + R10 = a cyclic phosphate;  
 R11 = -Y-(CH2)n-X-(CH2)m-SO3H, -Y'-(CH2)p-X'-(CH2)q-NR16NR17 or  
 -Z-(CH2)rQ;  
 Y = a bond or -O-;  
 X, X' = bond, -CON(R18)-, -N(R18)CO-, -O-, -S-, -S(O)- or -S(O)2-;  
 R18 = H or 1-4C alkyl;  
 R16, R17 = 1-4C alkyl optionally substituted by one hydroxy or  
 NR16R17 = pyrrolidino, piperidino, morpholino, thiomorpholino,  
 piperizino or N(1-4C lower alkyl)piperizino;  
 n = 4-9;  
 m, q = 1-5;  
 p = 2-9;  
 Z = a bond or -O-;  
 Q = -R19-CH2COOH, -CO-COOH or CON(R21)CH(R22)COOH;  
 R19 = -S-, -S(O)-, -S(O)2, -SO2N(R20)- or N(R20)SO2;  
 R20 = H or 1-4C alkyl, provided that the total number of C atoms in  
 R20 and (CH2)r is not greater than 10;  
 R21 = H and  
 R22 = H, CH3, -CH2COOH, -CH2CH2COOH, -CH2OH, -CH2SH, -CH2CH2SCH3 or  
 CH2Ph-OH, or  
 R21 = Me and  
 R22 = H, or  
 R21 + R22 = -CH-2CH2CH2-, or  
 -N(R21)CH(R22)COOH = -NHCH2CONHCH2COOH;  
 Ph-OH = hydroxyphenyl;  
 R24 = C, 1-2C double bond or O;  
 R25 = C(R15)CH2-R23, OH, OR26, OC(=O)R27, R26, COOH, C(=O)OR26,  
 CHOCH2OH, CHOCH2OR26, CHOCH2OC(=O)R27, CH2CH2OHCH2CH2OR26,  
 CH2CH2OC(=O)R27, CH2CN, CH2N3, CH2NH2, CH2NHR26, CH2N(R26)2, CH2OH,  
 CH2OR26, CH2O(C=O)R27, CH2O(P=O)(OH)2, CH2SC(=O)R27, CH2NC(=O)CHR28OR26,  
 C(=O)CHR28OC(=O)R27, or  
 R10 + R25 = =C(R28)2;  
 R26 = 1-6C (alkyl, branched alkyl, cycloalkyl, haloalkyl, aralkyl or  
 aryl);  
 R27 = R26 + OR26 and  
 R28 = H, 1-6C (alkyl, branched alkyl, cycloalkyl).  
 ACTIVITY - Ophthalmological; hypotensive.  
 MECHANISM OF ACTION - None given.  
 USE - Used for reducing IOP and controlling IOP spiking for treating  
 glaucoma and ocular hypertension.  
 ADVANTAGE - The angiostatic agent provides effective, long lasting  
 control of IOP and the other IOP lowering compound provides immediate  
 control of a patient's elevated IOP and hence less IOP spiking. The two  
 agents lower IOP provide the effect via differing mechanisms.  
 Dwg.0/0  
 FS  
 CPI  
 FA AB; GI; DCN  
 MC CPI: B01-A02; B01-B01; B01-B02; B01-B03; B01-B04; B04-H03; B07-E03;  
 B07-F01; B10-B03B; B14-F02B; B14-F02D; B14-N03

TECH UPTX: 20010328  
 TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred composition: The  
 angiostatic agent is e.g. 4,9(11)pregnadien-17-alpha,21-diol-3,20-dione-21-  
 acetate. The other IOP lowering agent is betaxolol.  
 The composition comprises 4,9(11)pregnadien-17-alpha,21-diol-3,20-dione-21-  
 acetate and timolol.

ABEX UPTX: 20010328  
 ADMINISTRATION - Administration is topical.

EXAMPLE - A composition was prepared comprising (in weight%): apraclonidine  
 HCl (0.58), 5beta-pregnane-3alpha,11beta,17alpha,21 tetrol-20-one  
 (tetrahydrocortisol) (1.0), Tyloxapol (0.01-0.05),  
 hydroxypropylmethylcellulose (0.5), benzalkonium chloride (0.01), NaCl  
 (0.8), edetate disodium (0.01), NaOH/HCl (to pH 7.4) and purified water  
 (to 100 ml).

L76 ANSWER 6 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 1999-405111 [34] WPIX

CR 1990-007032 [01]; 1990-253569 [33]; 1991-101860 [14]; 1993-182484 [22];  
 1999-131871 [11]

DNC C1999-119586

TI Angiostatic agents and their compositions.

DC B01

IN CLARK, A F

PA (ALCO-N) ALCON LAB INC; (CLAR-I) CLARK A F

CYC 25

PI WO 9932127 A1 19990701 (199934)\* EN 33 A61K031-57  
 RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE  
 W: AU BR CA JP MX

AU 9917142 A 19990712 (199950)

US 5990099 A 19991123 (200002) A61K031-58

EP 1039912 A1 20001004 (200050) EN A61K031-57

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

BR 9813684 A 20001010 (200055) A61K031-57

AU 734436 B 20010614 (200140) A61K031-57

MX 2000005276 A1 20010201 (200168) A61K031-56

JP 2001526233 W 20011218 (200203) 47 A61K045-00

EP 1039912 B1 20020807 (200259) EN A61K031-57

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

DE 69807115 E 20020912 (200268) A61K031-57

ES 2177112 T3 20021201 (200305) A61K031-57

ADT WO 9932127 A1 WO 1998-US25913 19981207; AU 9917142 A AU 1999-17142  
 19981207; US 5990099 A Cont of US 1988-264918 19881031, CIP of US  
 1989-419226 19891010, CIP of US 1990-559123 19900727, Cont of US  
 1992-941485 19920908, Cont of US 1994-349342 19941202, Cont of US  
 1996-643387 19960506, CIP of US 1997-990424 19971215, US 1997-994114  
 19971219; EP 1039912 A1 EP 1998-961956 19981207, WO 1998-US25913 19981207;  
 BR 9813684 A BR 1998-13684 19981207, WO 1998-US25913 19981207; AU 734436 B  
 AU 1999-17142 19981207; MX 2000005276 A1 MX 2000-5276 20000529; JP  
 2001526233 W WO 1998-US25913 19981207, JP 2000-525118 19981207; EP 1039912  
 B1 EP 1998-961956 19981207, WO 1998-US25913 19981207; DE 69807115 E DE  
 1998-607115 19981207, EP 1998-961956 19981207, WO 1998-US25913 19981207;  
 ES 2177112 T3 EP 1998-961956 19981207

FDT AU 9917142 A Based on WO 9932127; US 5990099 A Cont of US 4876250, Cont of  
 US 5371078, Cont of US 5698545; EP 1039912 A1 Based on WO 9932127; BR  
 9813684 A Based on WO 9932127; AU 734436 B Previous Publ. AU 9917142,  
 Based on WO 9932127; JP 2001526233 W Based on WO 9932127; EP 1039912 B1  
 Based on WO 9932127; DE 69807115 E Based on EP 1039912, Based on WO  
 9932127; ES 2177112 T3 Based on EP 1039912

PRAI US 1997-994114 19971219; US 1988-264918 19881031;  
 US 1989-419226 19891010; US 1990-559123 19900727;  
 US 1992-941485 19920908; US 1994-349342 19941202;  
 US 1996-643387 19960506; US 1997-990424 19971215

IC ICM A61K031-56; A61K031-57; A61K031-58; A61K045-00  
 ICS A61K031-573; A61K031-575; A61P027-06; A61P043-00; C07J001-00;  
 C07J003-00; C07J005-00; C07J013-00; C07J031-00; C07J041-00

AB WO 9932127 A UPAB: 20030121  
 NOVELTY - A new method for treating GLC1A glaucoma comprises  
 administration of an angiostatic agent.  
 DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a  
 composition for controlling GLC1A glaucoma comprising an angiostatic  
 agent, preferably of formula (A) or (B).  
 ACTIVITY - Angiostatic.  
 MECHANISM OF ACTION - Inhibition of GLC1A gene expression.  
 USE - The method is useful for treating GLC1A glaucoma.

Dwg.0/0  
 FS CPI  
 FA AB; GI; DCN  
 MC CPI: B01-A02; B01-A03; B01-D01; B01-D02; B14-N03  
 TECH UPTX: 19990825

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The  
 composition preferably contains 0.005 to 5%, especially 0.05 to 2%, of the  
 angiostatic agent.  
 Preferred Drugs: The angiostatic agent is preferably of formula (A) or  
 (B):  
 R1 = H, betab-CH3 or beta-C2H5;  
 R2 = F, C9-C11 double bond, C9-C11 epoxy, H or Cl;  
 R3 = H, OR26, OCOR27, halo, C9-C11 double bond, C9-C11 epoxy, =O, OH,  
 1-12C alkoxy, OCO(1-12C alkyl), OCOaryl, OCONR2 or OCOOR7;  
 aryl = furyl, thienyl, pyrrolyl or pyridyl (all optionally substituted by  
 up to 2 of 1-4C alkyl) or -(CH2)f-phenyl (optionally substituted by up to  
 3 of Cl, F, Br, 1-3C alkyl, 1-3C alkoxy, 1-3C thioalkyl, CC13, CF3, NH2 or  
 NHCOCH3;  
 f = 0-2;  
 R = H, 1-4C alkyl or phenyl;  
 R7 = aryl or 1-12C alkyl;  
 R4 = H, CH3, Cl or F;  
 R5 = H, OH, F, Cl, Br, CH3, phenyl, vinyl or allyl;  
 R6 = H or CH3;  
 R9 = CH2CH2OR26, CH2CH2OCOR27, H, OH, CH2, F, =CH2, CH2COOR28, OR26,  
 OCOR27 or OCOCH2COOR26;  
 R10 = -Cequivalent toCH, -CH=CH2, halo, CN, N3, OR26, OCOR27, H, OH, CH3  
 or a double bond between C-16 and C-17;  
 R12 = H or a double bond with R1 or R14;  
 R13 = halo, OR26, OCOR27, NH2, NHR26, NHCOR27, N(R26)2, NCOR27, N2, H, OH,  
 =O, OPO(OH)2 or OCO(CH2)tCOOH;  
 t = 2-6;  
 R14 = H or a double bond with R12;  
 R15 = H, =O or OH;  
 R23 = OH, OCOR11, OPO(OH)2 or OCO(CH2)tCOOH or with R10 = cyclic  
 phosphate;  
 R11 = -Y-(CH2)n-X-(CH2)mSO3H, -Y'-(CH2)p-X'-(CH2)q-NR16R17 or -Z(CH2)rQ;  
 Y = a bond or -O-;  
 Y' = a bond, -O- or -S-;  
 X, X' = a bond, CONR18, NR18CO, O, S, SO or SO2;  
 R18 = H or 1-4C alkyl;  
 R16, R17 = 1-4C alkyl optionally substituted by OH; or  
 R16-N-R17 = pyrrolidino, piperidino, morpholino, thiomorpholino,  
 piperazino or N(1-4C alkyl)piperazino;  
 n = 4-9;  
 m = 1-5;  
 p = 2-9;  
 q = 1-5;  
 Z = a bond or O  
 r = 2-9;  
 Q = -R19CH2COOH, -COCOOR or CONR21CHR22COOH;



r = 2-9;  
 Q = R19 = S, SO, SO<sub>2</sub>, SO<sub>2</sub>NR<sub>20</sub> or NR<sub>20</sub>SO<sub>2</sub>;  
 R<sub>20</sub> = H or 1-4C alkyl provided that the number of C-atoms in R<sub>20</sub> and (CH<sub>2</sub>)<sub>r</sub> is not greater than 10;  
 R<sub>21</sub> = H; and  
 R<sub>22</sub> = H, CH<sub>3</sub>, CH<sub>2</sub>COOH, CH<sub>2</sub>CH<sub>2</sub>COOH, CH<sub>2</sub>OH, CH<sub>2</sub>SH, CH<sub>2</sub>CH<sub>2</sub>SCH<sub>3</sub> or CH<sub>2</sub>(4-hydroxyphenyl); or  
 R<sub>21</sub> = CH<sub>3</sub>; and  
 R<sub>22</sub> = H; or  
 R<sub>21</sub>+R<sub>22</sub> = -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>- ; or  
 NR<sub>21</sub>CHR<sub>22</sub>COOH = NHCH<sub>2</sub>CONHCH<sub>2</sub>COOH;  
 provided that if R<sub>23</sub> is a phosphate it must form a cyclic phosphate, with R<sub>10</sub> when R<sub>13</sub> = =O, except for the compound in which  
 R<sub>1</sub> = beta-CH<sub>3</sub>;  
 R<sub>2</sub>+R<sub>3</sub> = C<sub>9</sub>-C<sub>11</sub> double bond;  
 R<sub>4</sub>, R<sub>6</sub> = H;  
 R<sub>12</sub>+R<sub>14</sub> = C<sub>4</sub>-C<sub>5</sub> double bond;  
 R<sub>5</sub> = alpha-F;  
 R<sub>9</sub> = beta-CH<sub>3</sub>;  
 R<sub>10</sub> = alpha-OH;  
 R<sub>13</sub>, R<sub>15</sub> = =O;  
 R<sub>23</sub> = OPO(OH)<sub>2</sub>;  
 R<sub>24</sub> = C, C<sub>1</sub>-C<sub>2</sub> double bond or O;  
 R<sub>25</sub> = CR<sub>15</sub>CH<sub>2</sub>R<sub>23</sub>, OH, OR<sub>26</sub>, OCOR<sub>27</sub>, R<sub>26</sub>, COOH, COOR<sub>26</sub>, CHOHCH<sub>2</sub>OH, CHOHCH<sub>2</sub>OR<sub>26</sub>, CHOHCH<sub>2</sub>OCOR<sub>27</sub>, CH<sub>2</sub>CH<sub>2</sub>OH, CH<sub>2</sub>CH<sub>2</sub>OR<sub>26</sub>, CH<sub>2</sub>CH<sub>2</sub>OCOR<sub>27</sub>, CH<sub>2</sub>CN, CH<sub>2</sub>N<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NHR<sub>26</sub>, CH<sub>2</sub>N(R<sub>26</sub>)<sub>2</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>OR<sub>26</sub>, CH<sub>2</sub>OCOR<sub>27</sub>, CH<sub>2</sub>OPO(OH)<sub>2</sub>, CH<sub>2</sub>OPO(OR<sub>26</sub>)<sub>2</sub>, CH<sub>2</sub>SH, CH<sub>2</sub>SR<sub>26</sub>, CH<sub>2</sub>SCOR<sub>27</sub>, CH<sub>2</sub>NCOR<sub>27</sub>, COCHR<sub>28</sub>OH, COCHR<sub>28</sub>OR<sub>26</sub>, COCHR<sub>28</sub>OCOR<sub>27</sub> or R<sub>25</sub>+R<sub>10</sub> = =C(R<sub>28</sub>)<sub>2</sub>;  
 R<sub>26</sub> = 1-6C alkyl, 3-6C cycloalkyl, 1-6C haloalkyl, aryl(1-6C alkyl) or aryl;  
 R<sub>27</sub> = R<sub>26</sub>+OR<sub>26</sub>;  
 R<sub>28</sub> = H, 1-6C alkyl or 3-6C cycloalkyl.  
 Most preferably the angiostatic agent is 4,9(11)-pregnadien-17alpha,21-diol-3,20-dione-21-acetate or 4,9(11)-pregnadien-17approximately,21-diol-3,20-dione.

ABEX

UPTX: 19990825

EXAMPLE - A typical composition contains angiostatic steroid (0.005 - 5%), tyloxapol (0.01 - 0.05%), HPMC (0.5%), benzalkonium chloride (0.01%), sodium chloride (0.8%), edetate disodium (0.01%), NaOH/HCl (to pH 7.4) and water (to 100ml).

=&gt; d his

(FILE 'HOME' ENTERED AT 16:07:03 ON 01 SEP 2004)  
 SET COST OFF

FILE 'REGISTRY' ENTERED AT 16:07:11 ON 01 SEP 2004  
 E ANECORTAVE/CN

L1 1 S E3,E4

SEL RN

L2 0 S E1/CRN

FILE 'HCAPLUS' ENTERED AT 16:08:35 ON 01 SEP 2004

L3 89 S L1

L4 10 S ANECORTAVE OR ANECORTAVE ACETATE OR NSC15475 OR NSC24345 OR N

L5 91 S L3,L4

L6 14 S L5 AND (EYE+OLD,NT,PFT,RT OR EYE, DISEASE+OLD,NT,PFT,RT)/CT

L7 9 S L5 AND EYE#/CW (L) DISEASE

L8 14 S L6,L7

FILE 'REGISTRY' ENTERED AT 16:11:26 ON 01 SEP 2004

L9 1 S 10184-70-0

L10 0 S 10184-70-0/CRN

FILE 'HCAPLUS' ENTERED AT 16:11:47 ON 01 SEP 2004

L11 45 S L9  
L12 1 S AL4940 OR AL 4940  
L13 45 S L11,L12  
L14 8 S L13 AND (EYE+OLD,NT,PFT,RT OR EYE, DISEASE+OLD,NT,PFT,RT)/CT  
L15 6 S L13 AND EYE#/CW (L) DISEASE  
L16 16 S L8,L14,L15  
L17 119 S L5,L13  
L18 0 S L17 AND AMD  
L19 3 S L17 AND MACUL? DEGENER?  
L20 3 S L17 AND EYE, DISEASE/CT (L) (MACULA OR DEGEN? OR SENIL?)  
L21 16 S L16,L19-L20  
L22 13 S L21 NOT L19,L20  
E EYE+ALL/CT  
L23 184018 S E26+OLD,NT,PFT,RT OR E27+OLD,NT,PFT,RT OR E28+OLD,NT,PFT,RT  
L24 11 S L17 AND L23  
L25 3 S L24 AND L19,L20  
L26 8 S L24 NOT L25  
L27 13 S L22,L26  
L28 1 S US20040127472/PN OR (WO2003-US20154 OR US2002-401220#)/AP,PRN  
E JERDAN J/AU  
L29 7 S E4-E6  
E ZILLIOX P/AU  
L30 2 S E4  
E ROBERTSON S/AU  
L31 151 S E3,E15,E16  
E ROBERTSON STELLA/AU  
L32 20 S E3-E5  
L33 2 S L17 AND L28-L32  
E ALCO/PA,CS  
E ALCOM/PA,CS  
L34 877 S E3-E8 OR ALCON?/PA,CS  
L35 12 S L17 AND L34  
L36 19 S L19-L22,L27,L28,L35  
L37 19 S L36 AND L3-L8,L11-L36  
L38 18 S L37 AND (PD<=20020805 OR PRD<=20020805 OR AD<=20020805)  
L39 2 S L19,L20 AND L38  
L40 3 S L19,L20,L39  
L41 16 S L37-L38 NOT L40  
SEL DN AN 15 16  
L42 14 S L41 NOT E1-E6  
L43 1 S L33,L35 NOT L40,L42  
L44 16 S L41,L42

FILE 'REGISTRY' ENTERED AT 16:23:44 ON 01 SEP 2004

FILE 'HCAPLUS' ENTERED AT 16:23:57 ON 01 SEP 2004

FILE 'EMBASE' ENTERED AT 16:25:24 ON 01 SEP 2004

L45 27 S L1 OR L9  
L46 33 S L4 OR L12  
L47 33 S L45,L46  
E EYE DISEASE/CT  
L48 31 S E3+NT AND L47  
E EYE/CT  
L49 10 S E3+NT AND L47  
L50 32 S L48,L49  
L51 23 S L47 AND MACUL? (L) DEGEN?  
L52 23 S L50 AND L51  
E MACULA DEGENERATION/CT  
E E3+ALL

L53 7817 S E2+NT  
L54 244 S E4+NT  
L55 250 S E6+NT  
L56 2790 S E8+NT  
L57 23 S L53-L56 AND L47  
L58 23 S L52,L57  
L59 6 S L58 AND PY<=2002  
L60 10 S L47 NOT L58

FILE 'EMBASE' ENTERED AT 16:29:04 ON 01 SEP 2004

FILE 'MEDLINE' ENTERED AT 16:29:31 ON 01 SEP 2004

L61 12 S L47  
E MACULA DEGENERATION/CT  
E RETINA MACULA DEGENERATION/CT  
E RETINAL MACULA DEGENERATION/CT  
E EYE DISEASE/CT  
E E5+ALL  
E E208+ALL  
L62 14366 S E4+NT  
L63 4 S L61 AND L62  
L64 5 S L61 AND MACUL?(L) DEGEN?  
L65 1 S L63,L64 AND PY<=2002

FILE 'MEDLINE' ENTERED AT 16:31:53 ON 01 SEP 2004

FILE 'BIOSIS' ENTERED AT 16:32:03 ON 01 SEP 2004

L66 29 S L47  
L67 16 S L66 AND MACUL?(L) DEGEN?  
L68 8 S L67 AND PY<=2002

FILE 'BIOSIS' ENTERED AT 16:34:26 ON 01 SEP 2004

FILE 'WPIX' ENTERED AT 16:34:36 ON 01 SEP 2004

L69 6 S L12/BIX OR L4/BIX  
E ANECORTAVE/DCN  
E ANECORTAVE/CN  
L70 1 S E3  
E RAOEF8/DCN  
E RAOEF8/DCN  
L71 11 S E3-E7  
L72 12 S L69,L71  
L73 5 S L72 AND (MACUL?(L) DEGEN?)/BIX  
L74 2 S L72 AND (AMD OR ARMD)/BIX  
L75 6 S L73,L74  
L76 6 S L72 NOT L75

FILE 'WPIX' ENTERED AT 16:37:51 ON 01 SEP 2004

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